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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 09/08/03

SUBJECT: PP# 1F06313 --**Human Health Risk Assessment for New Fungicide BAS 510 F (Common Name: Boscalid)** -- Proposal for Tolerances for Residues in/on Numerous Crops and Livestock Commodities.

DP Barcode:	D290022	PRAT Case:	
Submission No.:	S604279	Caswell No.:	none
Chemical#:	128008	Class:	Fungicide
Trade Name:	Endura™	EPA Reg#:	7969-ROT
	Pristine™		7969-ROO
	510 02 F Turf		7969-ROA
40 CFR:	§180.XXX		

TO: Dennis McNeilly/R. Keigwin
Registration Division (7505C)

FROM: Yan Donovan, Risk Assessor
Alan Levy, Toxicologist
Maxie Nelson, Chemist
Shi-Chi Wang, Environmental Health Specialist
RAB2/HED (7509C)

THRU: Michael Doherty, Chemist
Ed Budd, Toxicologist
Gary Bangs, Industrial Hygienist
RAB2/HED (7509C)

THRU: Richard A. Loranger, Branch Senior Scientist
RAB2/HED (7509C)

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The aggregate risk assessment was conducted by Yan Donovan, the residue chemistry data review was conducted by Maxie Nelson, the dietary risk assessment by Michael Doherty, the hazard characterization by Alan Levy, the occupational/residential exposure assessment by Shih-Chi Wang, Gary Bangs, and Margarita Collantes. Drinking water assessment was provided by Cheryl Sutton of the Environmental Fate and Effects Division (EFED).

1.0 EXECUTIVE SUMMARY

General Background:
BAS 510 F, 3-pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl), is a new fungicide active ingredient and this is its first petition (1F06313). The ISO common name is boscalid. Two formulated end-use products are proposed for use on crops: a Wettable Granule (WG) termed BAS 510 02 F (Endura™ Fungicide; EPA Reg. No. 7969-ROT) containing 70% BAS 510 F and a WG termed BAS 516 02 F (Pristine™ Fungicide; EPA Reg. No. 7969-ROO) containing a 2:1 mixture of BAS 510 F and BAS 500 F (pyraclostrobin) as co-active ingredients (25.2%:12.8%). In addition, there is a 70 WG end-use product termed BAS 510 02 F Turf Fungicide (EPA Reg. No. 7969-ROA) proposed for use only on golf course turfgrass (maximum 2.1 lbs ai/A/year). BAS 510 F is not currently planned for other residential uses.

Endura™ is intended for use on beans, berries, bulb vegetables, canola, carrots, fruiting vegetables, grapes, lettuce, peanuts, pistachios, potatoes, stone fruit, strawberries, tree nuts, *Brassica* vegetables (subgroups 5A and 5B), cucurbit vegetables, mint, edible peas, certain root vegetables, and sunflower. Pristine™ is intended for use on berries, bulb vegetables, carrots, grapes, pistachios, stone fruit, strawberries, and tree nuts. Application is via multiple, foliar, broadcast sprays at a seasonal rate of ca 0.9-1.8 lbs ai/A, depending on crop and target disease. Typically, retreatment intervals are 1-3 weeks and minimum PHIs are 0-30 days.

Hazard Assessment
BAS 510 F appeared to have effects on the thyroid and/or liver of several species. In a 90-day mouse study, there were increased liver weights and increased incidences in marked fatty change in the liver. These liver changes were not noted in the 18-month mouse study. In 90-day as well as in 2-year rat studies, there were thyroid changes (increase in weights and incidence of follicular cell hyperplasia and hypertrophy). The thyroid changes were considered to have been the result of liver adaptive responses. The 90-day and one-year dog studies showed increases in the levels of alkaline phosphatase as well as hepatic weights. In three mechanistic rat studies, the following were observed: increase in liver microsomal activity, induction of total cytochrome P450 activity, disruption of thyroid homeostasis by decreasing circulating T_3 and T_4 and increasing TSH (likely the result of hepatic microsomal glucuronyltransferase), and reversal of thyroid and liver effects with the cessation of test article administration (it was concluded that the induction of liver microsomal enzyme system resulted in increased glucuronidation of thyroxine, resulting in an increase in TSH secretion as a compensatory response of the physiological negative feedback system; increased TSH resulted in increased thyroid weight). There were little or no effects on body weights or body weight gains.

In the developmental toxicity studies, no effects were noted in rats; whereas, in the rabbit study, abortions or early delivery were observed at the highest dose tested (1000 mg/kg/day). Regarding the 2-generation reproduction study in rats, decreased body weights and/or body weight gains and hepatocyte degeneration were noted in males only. No reproductive effects were observed. The only effects noted in pups of both generations were decreases in body weights (both sexes of both generations) at the highest dose tested (>1000 mg/kg/day). There was no evidence of neurotoxicity based on an acute neurotoxicity study, a 90-day neurotoxicity study and a developmental neurotoxicity study (all in rats). There was no evidence of increased

susceptibility in the developmental rat study (Limit Dose). Qualitative, but not quantitative, increased susceptibility was noted in the developmental rabbit study as characterized by an increased incidence of abortions or early delivery at the highest dose tested (1000 mg/kg/day). It could not be ascertained if the abortions were the result of a treatment-related effect on either the dams, the fetuses or both. There was quantitative evidence of increased susceptibility in the two-generation reproduction rat study where decreases in body weights and body weight gains in male offspring were seen in the F_2 generation and in females from both generations at a dose that was lower than the dose that induced parental/systemic toxicity. Quantitative evidence of increased susceptibility was noted in the developmental neurotoxicity study in rats where decreases in pup body weights (PND 4) and body weight gains (PND 1-4) were seen in the absence of any maternal toxicity. The degree of concern is low for the qualitative evidence of susceptibility seen in the rabbit developmental study as the increased abortions or early delivery was seen only at the Limit Dose and the abortions may have been due to maternal stress. The degree of concern is low for the quantitative evidence of susceptibility seen in the two-generation reproduction study in rats because the decreases in body weight and body weight gains were seen only in the F_2 generation in males and in females in both generations. The degree of concern is low for the quantitative evidence of susceptibility in the developmental neurotoxicity study because the decreases in pup body weights seen on post natal days 1 through 4 (at no other time periods) were most likely due to maternal toxicity.

For the acute toxicity studies (oral, dermal, inhalation, primary eye irritation and primary skin irritation), the toxicity categories were III or IV. The guinea pig dermal sensitization assay was not acceptable because the concentration used for the challenge was inadequate.

The Cancer Assessment Review Committee (CARC) classified BAS 510 F as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", and, therefore, the quantification of human cancer risk is not recommended. The classification was based on data which were combined from two 2-year rat studies where males had a significant increasing trend and significant differences in pair-wise comparison with the controls for thyroid follicular cell adenomas. The increased incidence of these adenomas exceeded the historical control mean and range. This was supported by thyroid hypertrophy and hyperplasia of follicular cells, increased thyroid weights and mechanistic data. Combined study data for female rats showed only a borderline significant increasing trend for thyroid follicular cell adenomas. No increase over controls was noted in males or females for carcinomas. There was no increase in the incidence of any tumors of either sex in the 18-month mouse study. All mutagenic studies were negative with or without activation. Based on the overall weak evidence of carcinogenic effects, the CARC indicated that a dose-response assessment for cancer (either linear low-dose extrapolation or margin of exposure calculation) was not needed.

Dose Response Assessment and Food Quality Protection Act (FQPA) Decision

The special FQPA safety factor is reduced to 1X because the existing data indicate that there are no/low concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity. Conservative residue assumptions are used in the dietary risk assessments; there are no uses that will result in residential exposure except golf course and pick-your-own friuts; and the residue chemistry and environmental fate databases are relatively complete (evaluated by the risk

assessment team). A 1X database factor is to be applied to all dietary and residential exposure endpoints as there are no toxicology data gaps.

On September 5, 2002 and January 23, 2003, the HIARC selected endpoints for chronic dietary exposure (all populations), incidental oral short- and intermediate-term residential only, dermal (all durations) and inhalation (all durations). As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD). For all of the endpoints selected, liver and thyroid effects were chosen from the chronic toxicity study in rats, the carcinogenicity study in rats and the 1-year study in dogs. The NOAEL was 21.8 mg/kg/day. The uncertainty factor (UF) was 100. For the dermal route, the absorption rate was 15% relative to oral. For the inhalation route, the absorption rate was assumed to be 100%. The cPAD for the chronic dietary (all populations) exposure scenario = 0.218 mg/kg/day. The residential and occupational level of concern (LOC) for all routes is an MOE of 100.

Exposure Scenario	Dose	Endpoint	Study/Effect
Acute dietary	No appropriate endpoint identified	none	not applicable
Chronic dietary (all populations)	NOAEL = 21.8 mg/kg/day	cRfD and cPAD = 0.218 mg/kg/day	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Incidental oral (short- and intermediate-term residential only)	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential and occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Dermal (all durations) Absorption: 15%	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential), 100 (occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.
Inhalation (all durations) Absorption: 100%	Oral NOAEL = 21.8 mg/kg/day	Target MOE = 100 (residential), 100 (occupational)	Chronic rat, carcinogenicity rat and 1-year dog studies based on liver and thyroid effects.

Residential Exposure Estimates

The non-occupational dermal post-application exposure/risk for golfing was calculated by coupling turf transferable residue (TTR) values with activity specific transfer coefficient (Tc) values from the HED Science Advisory Council For Exposure Policy Number 3.1. The highest daily dose from golf turf exposure is 0.0008 mg/kg/day. All MOEs for the non-occupational dermal post-application exposure were greater than the target MOE of 100 and therefore risks did not exceed HED's level of concern.

Dietary Exposure Estimates

Residue Chemistry

HED's Metabolism Assessment Review Committee (MARC) concluded that parent BAS 510 F is the sole residue of concern for risk assessment and the tolerance expression for primary (target) crops and rotational (inadvertent or indirect residue) crops. The combined residues of parent

BAS 510 F, M510F 01, and M510F02 are the residues of concern for risk assessment and the tolerance expression in livestock matrices (see Attachment 3 for structures). Parent only is the residue of concern in drinking water assessment. MARC decisions are summarized in **Table 1**, below.

Matrix	Residue(s) for Tolerance Expression	Residue(s) for Risk Assessment
Target Crops	Parent	Parent
Rotational Crops	Parent	Parent
Livestock	Parent, M510F01, M510F02	Parent, M510F01, M510F02
Water	Not Applicable	Parent

[1] Both data collection and tolerance enforcement methods are available to measure these specific residues of concern in plant and livestock matrices.

The analytical enforcement method (GC/MS) for plants determines residues of BAS 510 F with an LOQ of 0.05 ppm. The Analytical Chemistry Branch (ACB) in BEAD has concluded that this method is acceptable for tolerance enforcement purposes in plant matrices without the need for an EPA validation. The analytical enforcement method for livestock determines residues of BAS 510 F, M510F01, and M510F02 (as M510F01). The reported LOQ for each analyte is 0.01 ppm in milk and 0.025 ppm in other animal matrices. ACB/BEAD has conducted a successful tolerance method validation on this method using beef liver and concluded that this method is acceptable for tolerance enforcement purposes in livestock matrices.

Adequate field trials were conducted to support the proposed uses using the maximum label rate and number of applications, and the minimum retreatment interval and PHI for each crop or crop group. Tier III extended field rotational crop studies resulted in detectable residues in a variety of crops planted into bare soil 14 days following the last of 3 applications totaling 1.8 lbs BAS 510 F ai/A. Appropriate indirect residue tolerances (ranging from 0.05 to 8.0 ppm) are being proposed.

Dietary Exposure Analysis

BAS 510 F chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The assessment used tolerance-level residue values (or higher in a few cases) for all of the commodities for which HED determined that tolerances are necessary. One hundred percent crop treated was assumed for all commodities. Empirical processing factors were used for all commodities except processed potato, peanut butter, and all dried foods (meat, potato, fruits, etc.) except prunes and raisins. Since empirical factors were not provided for those foods, the default factors from DEEM version 7.76 were used. Even with these highly conservative assumptions, the risk estimates are well below HED's level of concern.

Estimated exposures are less than 0.077 mg/kg/day (35% of the cPAD) for all population subgroups.

Drinking Water Exposure Estimates

EFED provided the Tier I estimated environmental concentrations (EECs) for BAS 510 F in surface water and in groundwater for use in the human health risk assessments. EFED used the simulation model FIRST to calculate the surface water EECs and used the simulation model SCI-GROW to calculate the groundwater EEC. Because BAS 510 F is a new chemical, monitoring data were not available. For the surface water and groundwater assessments, the application rate for turf was used, which represents the highest seasonal application rate (2.1 lb a.i./A/season) on the proposed labels. It is noted that the highest single application rate (0.547 lb a.i./A), associated with the use on fruiting vegetables, did not result in EEC values higher than those from turf use (since the proposed total seasonal application rate for fruiting vegetables is only 1.1 lb a.i./A/season). The EEC for surface water is 25.6 ug/L for chronic exposure. For ground water, the EEC is 0.57 ug/L for chronic exposure.

Aggregate Exposure Scenarios and Risk Conclusions

Short- term aggregate risk

Postapplication exposures from the proposed use on golf course is considered short- term and applies to adults and youth. Therefore, a short-term aggregate risk assessment was conducted. Since all endpoints are from the same study, exposures from different routes can be aggregated. The short term aggregate risk assessment takes into account average exposure estimates from dietary consumption of BAS 510 F (food and drinking water) and exposures from non-occupational uses (golf course). The aggregate MOE from food and non-occupational exposure is 1200, and the calculated short term DWLOC is 6000 ppb. Compared to EFED's surface and ground water EECs, the DWLOC is considerably greater and therefore, the short- term aggregate risk did not exceed HED's level of concern.

Chronic aggregate risk

The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of BAS 510 (food and drinking water) and residential uses. Since the exposure from turf grass (golf course) is considered short term, the chronic aggregate assessment included food and drinking water only. The calculated chronic DWLOCs for exposure to BAS 510 in drinking water range from 1400 to 7000 µg/L (ppb). EECs generated by EFED are less than HED's calculated chronic DWLOCs. Therefore, the chronic aggregate risk associated with the proposed use of BAS 510 does not exceed HED's level of concern for the general U.S. population or any population subgroup.

Occupational Exposure Estimates

Occupational exposures for the proposed uses were assessed. No data regarding the number of exposure days per year were provided. However, due to the frequency of applications and application interval, EPA assumes that both handlers involved in applications and workers performing post-application activities would be exposed for less than 6 months per year (i.e., short- and intermediate- term exposure).

Since no chemical-specific data for assessing human exposures during pesticide handling activities were submitted to the Agency in support of the registration of BAS 510F, HED used surrogate data from the Pesticide Handlers Exposure Database (PHED) Version 1.1. Defaults established by the Health Effects Division (HED) Science Advisory Council for Exposure were used for acres treated per day and body weight. Occupational handler assessments were based primarily on surrogate unit exposures from the PHED, as presented in the PHED Surrogate Exposure Guide (8/98). All MOEs for the handlers performing agricultural crop activities were greater than the target of 100 at the baseline level (ranging from 460 to 31,000). All MOEs for the handlers performing golf course turfgrass activities were also greater than the target of 100 at the baseline level (ranging from 7,300 to 27,000).

Four chemical-specific DFR studies and one TTR study were submitted to support the evaluation of post-application exposures/risks. PMRA performed primary reviews on the studies and HED performed secondary reviews. HED concurred with the DFR study reviews done by PMRA The occupational post-application exposure/risk were calculated by coupling crop specific DFR values with activity specific transfer coefficient (Tc) values from the HED Science Advisory Council For Exposure Policy Number 3.1. Except for grapes with girdling, all post-application MOEs were greater than the target MOE of 100. The MOE for grapes with girdling was 95 on the day of application. The MOE did not reach the target MOE of 100 till day 9. Due to the statistical uncertainty in estimating the MOE, 95 is considered equivalent to the target of 100 for risk assessment in this case. Therefore, the Restricted Entry Interval (REI) may be based on acute toxicity of the active ingredient. HED does not concur with the proposed 4-hour Restricted Entry Interval (REI) because the determination as to whether BAS 510F is or is not a dermal sensitizer could not be made. **HED recommends use of the worker protection standard (WPS) required 12 hour REI based on acute toxicity categories.** Should an acceptable dermal sensitizer study be submitted in the future, HED will revisit the REI issue.

Recommendations:

HED concludes that there is a reasonable certainty that no harm will result to the U.S. Population including infants and children from short-term and chronic aggregate exposure to BAS 510 F residues. **HED notes that although pome fruit and hops from petition PP# 2F06434 were included in the dietary analysis, these residue data have not been reviewed by HED, and the worker exposure assessment associated with these uses has not been conducted. HED does not recommend tolerances for pome fruit and hops at this time.** Contingent on the submissions of data to fulfill identified data gaps under Section 8.0, HED has no objection to conditional registration and the establishment of permanent tolerances for the residues of BAS 510 F, expressed as parent, (plus metabolites in the case of livestock commodities), in or on **the following:**

BAS 510 F: HED RECOMMENDED TOLERANCES ———— PRIMARY CROPS	
Tolerance Expression: 3-pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)	
Commodity Expression	**PPM**
Vegetable, root, subgroup 1A, except sugar beet, garden beet, radish, and turnip	0.7

Vegetable, tuberous and corm, subgroup 1C	0.05
Vegetable, bulb, group 3	3.0
Lettuce, head Lettuce, leaf	6.5 11.0
Vegetable, *Brassica* leafy, head and stem, subgroup 5A	3.0
Vegetable, *Brassica* leafy, leafy greens, subgroup 5B	18.0
Vegetable, legume, edible podded, subgroup 6A	1.6
Vegetable, legume, succulent shelled pea and bean, subgroup 6B, except cowpea	0.6
Vegetable, legume, dried shell pea and bean (except soybean), subgroup 6C, except cowpea, field pea, and grain lupin	2.5
Vegetable, fruiting, group 8	1.2
Vegetable, cucurbit, group 9, except cucumber Cucumber	1.6 0.20
Fruit, stone, group 12	1.7
Berries, group 13	3.5
Nut, tree, group 14	0.70
Almond, hulls	3.0
Pistachio	0.70
Grape	3.5
Grape, raisin	8.5
Strawberry	1.2
Peanut	0.05
Peanut, meal	0.15
Peanut, refined oil	0.15
Canola, seed Canola, refined oil	3.5 5.0
Sunflower, seed	0.60
Peppermint, tops Spearmint, tops	30.0 30.0

BAS 510 F: HED RECOMMENDED TOLERANCES ———— ROTATIONAL CROPS	
Tolerance Expression: 3-pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)	
Commodity Expression	**PPM**
Beet, garden, roots Radish, roots Turnip, roots	1.0 1.0 1.0

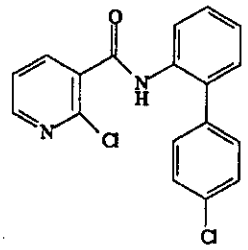
Beet, sugar, roots	1.0
Vegetable, root and tuber, leaves, group 2	1.0
Vegetable, leafy, group 4, except lettuce	1.0
Vegetable, legume, foliage, group 7, forage Vegetable, legume, foliage, group 7, hay Vegetable, legume, foliage, group 7, vines	1.5 2.0 0.05
Grain, cereal, group 15	0.20
Rice, hulls	0.50
Grain, cereal, forage, fodder and straw, group 16, forage Grain, cereal, forage, fodder and straw, group 16, straw Grain, cereal, forage, fodder and straw, group 16, fodder	2.0 3.0 1.5
Grass, forage, fodder, and hay, group 17, forage Grass, forage, fodder, and hay, group 17, hay Grass, forage, fodder, and hay, group 17, straw Grass forage, fodder, and hay, group 17, seed screenings	2.0 8.0 0.30 0.20
Animal feed, nongrass, group 18, forage Animal feed, nongrass, group 18, hay Animal feed, nongrass, group 18, seed	1.0 2.0 0.05
Cotton, undelinted seed	0.05
Cotton, gin byproducts	0.30
Soybean, seed	0.10
Soybean, hulls	0.20
Cowpea, seed Lupin, grain, grain Pea, field, seed	0.1 0.1 0.1
Flax, seed	3.5

BAS 510 F: HED RECOMMENDED TOLERANCES ———— LIVESTOCK COMMODITIES	
Tolerance Expression: 3-pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl) and metabolites M510F01 [2-chloro-N-(4'-chloro-5-hydroxy-biphenyl-2-yl) nicotinamide] and M510F02 [glucuronic acid conjugate of M510F01]	
Commodity Expression	**PPM**
Milk	0.10
Cattle, meat	0.10
Cattle, fat	0.30
Cattle, meat byproducts	0.35
Egg	0.02
Poultry, meat	0.05
Poultry, fat	0.05

Poultry, meat byproducts	0.10
Goat, meat	0.10
Goat, fat	0.30
Goat, meat byproducts	0.35
Hog, meat	0.05
Hog, fat	0.10
Hog, meat byproducts	0.10
Horse, meat	0.10
Horse, fat	0.30
Horse, meat byproducts	0.35
Sheep, meat	0.10
Sheep, fat	0.30
Sheep, meat byproducts	0.35

2.0 PHYSICAL/CHEMICAL PROPERTIES CHARACTERIZATION

Common Name:	Boscalid (ISO)
IUPAC Name:	2-Chloro-N-(4'-chlorobiphenyl-2-yl)nicotinamide
CAS Name:	3-Pyridinecarboxamide, 2-chloro-N-(4'-chloro[1,1'-biphenyl]-2-yl)-
CAS Number:	188425-85-6
Company Name:	BAS 510 F
Other Synonyms:	BASF Registry No. 300355
PC Code:	128008
Chemical Class/Type:	Carboxamide aka anilide /Fungicide
Mode of Action:	Acts in the fungal cell by inhibiting mitochondrial respiration and subsequent production of ATP and by inhibiting the succinate-ubiquinone oxidase reductase system in Complex II of the mitochondrial electron transport chain.
Impurities of Concern:	Yes, as microcontaminants (for details, see Product Chemistry review D285692, S. Mathur, 10/31/02, CBI).
Systemic (Yes/No):	Yes
Chemical Structure:	



Molecular Formula:	$C_{18}H_{12}Cl_2N_2O$
Molecular Weight:	343.21
Appearance:	White powder (TGAI); White crystalline (PAI)
Melting Point:	143.4-143.6° C (TGAI); 142.8-143.8°C (PAI)
Boiling Point:	Not required for a solid
Density:	1.394 g/cm^3 (TGAI); 1.381 g/cm^3 (PAI)
Water Solubility:	4.64 mg/L (PAI at 20°C)
Solvent Solubility:	PAI at 20°C in: acetone (16-20 g/100 ml); acetonitrile (4-5 g/100 ml); methanol (4-5 g/100ml); ethylacetate (6.7-8 g/100 ml); dichloromethane (20-25g/100 ml); toluene (2-2.5 g/100ml); 1-octanol (<1g/100ml).
Vapor Pressure:	7×10^{-9} hPa (PAI at 20°C); 2×10^{-8} hPa (PAI at 25°C)
pK_a:	No dissociation in water. The compound is not expected to dissociate.
K_{ow}:	Octanol/water partition coefficient (log K_{ow}) of PAI at 21°C=2.96 (= K_{ow} of 915). Because the compound does not dissociate, the value of K_{ow} is not pH dependent.

3.0 HAZARD CHARACTERIZATION (Attachment 1, HED HIARC report of 03/07/03, TXR No. 0051613)

3.1 Hazard Profile

Table 2. Acute Toxicity Profile - BAS 510 F Technical

Test Material	GDLN	Study Type	MRID	Results	Tox Category
Technical	870.1100	Acute Oral - rat	45404814	LD_{50} > 5000 mg/kg	IV
Technical	870.1200	Acute Dermal - rat	45404815	LD_{50} > 2000 mg/kg	III
Technical	870.1300	Acute Inhalation	45404816	LC_{50} (M & F): > 6.7 mg/L	IV
Technical	870.2400	Primary Eye Irritation	45404817	Not irritating to the eye	IV
Technical	870.2500	Primary Dermal Irritation	45404818	Not irritating to the skin	IV
Technical	870.2600	Dermal Sensitization	45404819	Study unacceptable as challenge dose was inadequate	N/A

Table 3. Toxicity Profile of BAS 510 F Technical.		
Guideline No.	Study Type	Results
870.3100	90-Day oral toxicity rodents (rats)	**NOAEL**: 34/159 mg/kg/day (M/F) **LOAEL**: 137/395 mg/kg/day (M/F): M = increases in absolute and relative thyroid weights and increased incidence of thyroid hyperplasia as well as follicular epithelial hypertrophy; F = increases in absolute and relative thyroid weights.
870.3100	90-Day oral toxicity rodents (mice)	**NOAEL**: 197/2209 mg/kg/day (M/F) **LOAEL**: 788/2209 mg/kg/day (M/F): M = increased liver weights and increased incidence of marked fatty change in the liver; F = not attained
870.3150	90-Day oral toxicity in nonrodents (dogs)	**NOAEL**: 7.6/8.1 mg/kg/day (M/F) **LOAEL**: 78.1/81.7 mg/kg/day (M/F): M = increased alkaline phosphatase activity and hepatic weights; F = increased alkaline phosphatase activity and hepatic weights.
870.3200	21/28-Day dermal toxicity (rats)	**NOAEL**: 1000 mg/kg/day (HDT) **LOAEL**: >1000 mg/kg/day
870.3700	Prenatal developmental in rodents (rats)	**Maternal NOAEL**: 1000 mg/kg/day **Maternal LOAEL**: cannot be established **Developmental NOAEL**: 1000 mg/kg/day **Developmental LOAEL**: cannot be established
870.3700	Prenatal developmental in nonrodents (rabbit)	**Maternal NOAEL**: 300 mg/kg/day **Maternal LOAEL**: 1000 mg/kg/day based on abortions or early delivery. **Developmental NOAEL**: 300 mg/kg/day **Developmental LOAEL**: 1000 mg/kg/day based on abortions or early delivery.

Table 3. Toxicity Profile of BAS 510 F Technical.		
Guideline No.	Study Type	Results
870.3800	Reproduction and fertility effects (rat)	**Parental systemic NOAEL**:112.6/1180.8 mg/kg/day (M/F) **Parental systemic LOAEL**:1165.0/>1180.8 mg/kg/day (M/F) decreased body weight and body weight gain (F_1) as well as hepatocyte degeneration F_0 and F_1) in males only. **Offspring systemic NOAEL**:11.2/115.8 mg/kg/day (M/F) **Offspring systemic LOAEL**:112.6/1180.8 mg/kg/day (M/F): decreased body weight for F_2 pups in males and females of both generations. **Reproductive NOAEL**:1165.0/1180.8 mg/kg/day (M/F) **Reproductive LOAEL**:>1165.0/1180.8 (M/F)
870.4100a	Chronic toxicity rodents (rat)	**NOAEL**: 21.9/30.0 mg/kg/day (M/F) **LOAEL**: 110.0/150.3 mg/kg/day (M/F): M = thyroid toxicity (weights and microscopic changes); F = thyroid toxicity (weights and microscopic changes). Thyroid follicular cell adenomas: M = 0/20, 0/20, 2/20,1/20; F = 0/20, 0/20, 1/20,0/20.
870.4100	Chronic toxicity dogs	**NOAEL**: 21.8/22.1mg/kg/day (M/F) **LOAEL**:57.4/58.3 mg/kg/day (M/F): M = elevated ALP activities and elevated hepatic weights; F = no effects
870.4200	Carcinogenicity rats	**NOAEL**: 23.0/29.7 mg/kg/day (M/F) **LOAEL**: 116.1/155.6 mg/kg/day (M/F): M = increased incidence of thyroid follicular cell hyperplasia and hypertrophy; F = decrease in body weight gain and increased incidence of thyroid follicular cell hyperplasia and hypertrophy. Thyroid follicular cell adenomas: M = 0/50, 0/50, 1/50, 4/50; F = 0/50, 1/50, 0/50, 3/50.
870.4200	Carcinogenicity mice	**NOAEL**:65/443 mg/kg/day (M/F) **LOAEL**: 331/1804 mg/kg/day (M/F): M = decreases in body weight and body weight gains; F = decreases in body weight and body weight gains. No evidence of carcinogenicity.
870.4300	Chronic feeding/Carcinogenicity rat	See 870.4100a and 870.4200.

Table 3. Toxicity Profile of BAS 510 F Technical.		
Guideline No.	**Study Type**	**Results**
870.5100	Gene Mutation bacterial reverse mutation assay	Negative without and with S-9 activation up to limit dose of 5000 µg/plate.
870.5300	*In vitro* mammalian cell forward gene mutation assay (CHO cells/HGPRT locus)	Negative without and with S-9 activation up to the limit of solubility of 25 µg/mL.
870.5375	*In vitro* mammalian cytogenetics assay in Chinese hamster V79 cells	Negative without and with S-9 activation up to 3500 µg/mL with precipitation showing at concentrations of 100 µg/mL and higher.
870.5395	Cytogenetics - mammalian erythrocyte micronucleus test in the mouse	Negative at doses up to 2000 mg/kg.
870.5500	*In vitro* unscheduled DNA synthesis (primary rat hepatocytes)	Negative response up to 50 µg/mL. Cytotoxicity at 100-500 µg/mL.
870.6200	Acute neurotoxicity screening battery (rat)	**NOAEL:**2000/1000 mg/kg/day (M/F) **LOAEL:** >2000/2000 mg/kg/day (M/F): F = piloerection
870.6200	Subchronic neurotoxicity screening battery (rat)	**NOAEL:**1050.0/1272.5 mg/kg/day (M/F) **LOAEL:** >1050.0/1272.5 mg/kg/day (M/F)
870.6300	Developmental neurotoxicity (rat)	**Maternal NOAEL:**1442 mg/kg/day **Maternal LOAEL:** >1442 mg/kg/day **Offspring NOAEL:** 14 mg/kg/day **Offspring LOAEL:** 147 mg/kg/day (decreased body weights on PND 4 and decreased body weight gain on PNDs 1-4)

Table 3. Toxicity Profile of BAS 510 F Technical.		
Guideline No.	**Study Type**	**Results**
870.7485	Metabolism and pharmacokinetics (rat)	BAS 510 F was readily absorbed and excreted following single oral 50 mg/kg; at single 500 mg/kg or 15 doses of 500 mg/kg, absorption was saturated. Excretion mainly by feces (80-98%). Biliary excretion 40-50% of fecal activity at 50 mg/kg, 10% at 500 mg/kg. Urine, about 16% at 50 mg/kg, 3-5% at 500 mg/kg. Absorption about 56% at 50 mg/kg and 13-17% at 500 mg/kg. Excretory patterns similar by gender or radiolabel position. Metabolites (hydroxylation and conjugation products) were consistent with Phase I oxidation reactions followed by Phase II conjugation with glucuronic acid or sulfate, or by conjugation of the parent with glutathione with cleavage to sulfate metabolites.
870.7600	Dermal Penetration (rat)	Maximum % absorption: 0.01 mg/cm^2 = 10.93 (24 hour exposure, 24 hour sacrifice) 0.10 mg/cm^2 = 3.76 (24 hour exposure, 24 hour sacrifice) 1.00 mg/cm^2 = 1.48 (10 hour exposure, 72 hour sacrifice)
none	SPECIAL STUDY: Hepatic enzyme induction (rat)	1. hypertrophy of zone III hepatocytes 2. >20% increase in liver weight 3. increase in CYP450 activity 4. slight to extensive microscopic SER proliferation 5. not a peroxisome proliferator 6. enzymes in CYP450 subfamily not induced 7. no notable microscopic increase in size or number of peroxisomes CONCLUSION: inducer of total CYP450 activity
none	SPECIAL STUDY: Hormone and enzyme induction (rat)	1. slight (statistically significant) decrease in circulating T_3 and T_4 only in males 2. increase in circulating TSH levels both sexes 3. increase in all 3 liver microsomal glucuronyltransferases CONCLUSION: disruption of thyroid homoeostasis by decreasing circulating T_3 and T_4 and increasing TSH; likely the result of hepatic microsomal glucuronyltransferase induction

Table 3. Toxicity Profile of BAS 510 F Technical.		
Guideline No.	Study Type	Results
none	SPECIAL STUDY: Reversibility study (dietary): 4-week administration followed by 4 weeks recovery or 13 weeks recovery (rat)	4 weeks dosing: at 2500 and 15000 ppm: increase in TSH (68% and 87%); increase in absolute and relative thyroid weights, hypertrophy of thyroid follicular epithelial cells and diffuse follicular hyperplasia, increase in absolute and relative liver weights and centrilobular hypertrophy as well as liver portal fatty changes. 4 weeks dosing + 4 weeks recovery: no increases in TSH; increase in absolute and relative thyroid weights; thyroid hypertrophy and hyperplasia decreased to control values; all liver effects reversed to control. 4 weeks dosing + 13 weeks recovery: no increases in TSH; increase in absolute and relative thyroid weights; thyroid hypertrophy and hyperplasia decreased to control values; all liver effects reversed to control. CONCLUSION: induction of liver microsomal enzyme system resulting in increased glucuronidation of thyroxine, resulting in an increase in TSH secretion as a compensatory response of the physiological negative feedback system; increased TSH resulted in increased thyroid weight.

BAS 510 F is a new fungicide. The primary targets are the liver and the thyroid (indirectly from liver adaptive response). In acute studies, there is relatively low toxicity (toxicity categories III or IV for oral, dermal, inhalation, primary eye irritation and primary skin irritation). In a dermal sensitization study in guinea pigs, the study was unacceptable because the concentration used for the challenge was inadequate.

In subchronic and chronic feeding studies in rats, mice and dogs, BAS 510 F generally caused decreased body weights and body weight gains (primarily in mice) and effects on the liver (increase in weights, changes in enzyme levels and histopathological changes) as well as on the thyroid (increase in weights and histopathological changes).

In a developmental toxicity study in rats, no developmental toxicity was observed in the fetuses at the highest dose tested (Limit Dose). No effects were noted in the dams in this study. In a developmental toxicity study in rabbits, an increased incidence of abortions or early delivery was

observed at the Limit Dose. Since it could not be determined whether the abortions or early delivery were due to maternal toxicity or due to an effect on reproductive/developmental mechanisms, the LOAELs and NOAELs in this study for both maternal and developmental toxicity were considered to be the same. The does (maternal toxicity) and fetuses (developmental toxicity) were considered to be equally sensitive to the test material. This study does not indicate an increased susceptibility of fetuses, as compared to does. In a 2-generation reproduction study in rats, the NOAEL for parental toxicity was based on decreased body weight and body weight gain as well as hepatocyte degeneration. The NOAEL for offspring toxicity was based on decreased body weights and body weight gains for the pups. No reproductive toxicity was observed in this study at the highest dose tested. There was no evidence of susceptibility in the developmental rat study. There was evidence of qualitative (not quantitative) susceptibility in the developmental rabbit study as characterized by an increased incidence of abortions or early delivery at the highest dose tested. There was quantitative evidence of increased susceptibility in the two-generation reproduction study in rats, where decreases in body weights and body weight gains in male offspring were seen at a dose that was lower than the dose that induced parental/systemic toxicity. There was quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats, where decreases in pup body weights (PND 4) and body weight gains (PND 1-4) were seen in the absence of any maternal toxicity.

In a two-year chronic toxicity study and a two-year carcinogenicity study in male and female rats, the combined data showed that, for thyroid follicular cell adenomas, males had a significant increasing trend and significant differences in the pair-wise comparison of the highest dose group, when compared with controls. There was no treatment-related increase in thyroid follicular cell carcinomas. The increased incidence of the thyroid follicular cell adenomas exceeded the historical control mean and range. The increase in thyroid follicular cell adenomas appeared to be treatment-related in males. This was supported by thyroid hypertrophy and hyperplasia of follicular cells at the same dose as well as increased thyroid weights plus mechanistic data. Regarding females, combined data from the two rat studies indicated that there was only a borderline increasing trend for thyroid follicular cell adenomas. No carcinomas were observed in females. The mouse carcinogenicity study was negative. BAS 510 F was tested in five mutagenicity studies and was found to be negative in all of them. Based on this weak evidence of carcinogenic effects, BAS 510 F is classified as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", according to the EPA *Draft Proposed Guidelines for Carcinogen Risk Assessment* (July 2, 1999).

In neither an acute nor a subchronic neurotoxicity study in rats was there evidence of a neurotoxic effect at the Limit Dose. In a developmental neurotoxicity study in rats, there were no neurotoxic effects observed at the Limit Dose. No neurotoxic observations were noted in any of the other studies in any species.

In metabolism and pharmacokinetic studies, BAS 510 F was readily absorbed and excreted following a single oral dose of 50 mg/kg. At single 500 mg/kg or 15 doses of 500 mg/kg, absorption was saturated. Excretion was mainly by feces (80-98%). Biliary excretion was 40-50% of fecal activity at 50 mg/kg and 10% at 500 mg/kg. Urinary content was about 16% at 50 mg/kg and 3-5% at 500 mg/kg. Absorption was about 56% at 50 mg/kg and 13-17% at 500 mg/kg. Excretory patterns were similar by gender or radiolabel position. Metabolites (hydroxylation and

conjugation products) were consistent with Phase I oxidation reactions followed by Phase II conjugation with glucuronic acid or sulfate, or by conjugation of the parent with glutathione with cleavage to sulfate metabolites.

A dermal absorption study in rats is available. Doses used were 0.01, 0.10 and 1.0 mg/cm^2. The maximum percent absorptions were as follows: 0.01 = 10.93 (24 hour exposure, 24 hour sacrifice); 0.10 = 3.76 (24 hour exposure, 24 hour sacrifice); and 1.00 = 1.48 (10 hour exposure, 72 hour sacrifice). The total amount of absorption was 15% as represented by 11% being absorbed at 24 hours plus 4% found as bound residue on the skin.

3.2 FQPA Considerations

The HIARC met on September 5, 2002 and January 23, 2003 to evaluate BAS 510 F according to the February 2002 OPP 10X Guidance Document. The HIARC concluded that the toxicology database for BAS 510 F was complete for FQPA purposes. A complete complement of acceptable developmental, reproduction, developmental neurotoxicity and mammalian neurotoxicity studies are available. Based on the weight-of-evidence considerations, HIARC determined that there is a low concern for pre- and/or post-natal toxicity resulting from exposure to BAS 510 F.

There was no evidence of increased susceptibility in the developmental rat study as no developmental toxicity was seen at the highest dose tested (Limit Dose).

There was evidence of qualitative (not quantitative) increased susceptibility in the developmental rabbit study as characterized by an increased incidence of abortions or early delivery at the highest dose tested (1000 mg/kg/day). It could not be ascertained if the abortions were the result of a treatment-related effect on either the dams, the fetuses or both.

There was quantitative evidence of increased susceptibility in the two-generation reproduction study in rats, where decreases in body weights and body weight gains in male offspring were seen in the F_2 generation at a dose that was lower than the dose that induced parental/systemic toxicity. The offspring NOAEL was 10.1/106.8 mg/kg/day in males and females, respectively, and the parental/systemic NOAEL was 101.2/1062.0 mg/kg/day in males and females, respectively.

There was quantitative evidence of increased susceptibility in the developmental neurotoxicity study in rats, where decreases in pup body weights (PND 4) and body weight gains (PND 1-4) were seen in the absence of any maternal toxicity. The offspring toxicity NOAEL was 14 mg/kg/day and the maternal NOAEL was 1442 mg/kg/day.

The HIARC concluded that the degree of concern is low for the qualitative evidence of susceptibility seen in the rabbit developmental study as the increased abortions or early delivery was seen only at the Limit Dose and not at the lower levels (i.e. a high-dose effect) and the abortions may have been due to maternal stress.

The HIARC concluded that the degree of concern is low for the quantitative evidence of susceptibility seen in the two-generation reproduction study in rats because the decreases in body weight and body weight gains were seen primarily in the F_2 generation. These may have been due to

exposure of the parental animals to high doses (above the Limit Dose). The dose selected for chronic dietary and non-dietary exposure risk assessments would address the concern for the body weight effects.

The HIARC concluded that the degree of concern is low for the quantitative evidence of susceptibility seen in the developmental neurotoxicity study because the decreases in pup body weights seen on post natal days 1 through 4 (and not at any other time periods) were most likely due to maternal toxicity (the maternal animals were exposed to a very high dose exceeding the limit dose, i.e., 1442 mg/kg/day); and no treatment-related effects on body weight, body weight gain or any other parameter were noted at post natal day 21.

The HIARC concluded that there are no residual uncertainties for pre- and post-natal toxicity as the degree of concern is low for the susceptibility seen in the above studies, and the dose and endpoints selected for the overall risk assessments will address the concerns for the body weight effects seen in the offspring. Although the dose selected for overall risk assessments (21.8 mg/kg/day) is higher than the NOAELs in the two-generation reproduction study (10.1 mg/kg/day) and the developmental neurotoxicity study (14 mg/kg/day), these differences are considered to be an artifact of the dose selection process in these studies. For example, there is a 10-fold difference between the LOAEL (106.8 mg/kg/day) and the NOAEL (10.1 mg/kg/day) in the two generation reproduction study. A similar pattern was seen with regard to the developmental neurotoxicity study, where there is also a 10-fold difference between the LOAEL (147 mg/kg/day) and the NOAEL (14 mg/kg/day). There is only a 2-3 fold difference between the LOAEL (57 mg/kg/day) and the NOAEL (21.8 mg/kg/day) in the critical study used for risk assessment. Because the gap between the NOAEL and LOAEL in the 2-generation reproduction and developmental neurotoxicity studies was large and the effects at the LOAELs were minimal, the true no-observed-adverse-effect-level was probably considerably higher. Therefore, the selection of the NOAEL of 21.8 mg/kg/day from the 1-year dog study is conservative and appropriate for the overall risk assessments. In addition, the endpoints for risk assessment are based on thyroid effects seen in multiple species (mice, rats and dogs) and after various exposure durations (subchronic and chronic exposures) which were not observed at the LOAELs in either the two-generation reproduction or the developmental neurotoxicity studies. Based on these data, the HIARC concluded that there are no residual uncertainties for pre- and post-natal toxicity.

For BAS 510 F, a comparative thyroid assay was not deemed to be necessary. Levels of thyroid related hormones were measured only in the mode of action studies performed in rats (not in the subchronic or chronic studies in rats, mice or dogs). The mode of action studies in rats indicate that BAS 510 F has a direct effect upon the liver and that the thyroid effects are secondary. A reversibility study in rats indicated that both liver and thyroid parameters returned to control values after the animals were placed on control diet. Absolute and/or relative thyroid weights were elevated in rats and dogs, but only at doses >100 mg/kg/day. There was no histopathology in either mice or dogs which indicated thyroid changes. Because BAS 510 F appears to act directly on the liver (liver microsomal enzyme changes) with the thyroid effects being secondary, it is considered that the above data do not indicate a need for a comparative thyroid assay.

The HIARC determined that the special FQPA Safety Factor can be removed (1X) because there is no evidence of susceptibility following *in utero* exposure to rats and there is low concern and no residual uncertainties in the developmental toxicity study in rabbits, in the 2-generation reproduction

study or in the developmental neurotoxicity study after establishing toxicity endpoints and traditional uncertainty factors to be used in the risk assessment. The BAS 510 risk assessment team evaluated the quality of the exposure data; and, based on these data, recommended that the special FQPA SF be reduced to 1x. The rationales from the exposure side are:

- The dietary food exposure assessment utilizes proposed tolerance level or higher residues and 100% CT information for all commodities. By using these screening-level assessments, chronic exposures/risks will not be underestimated.

- The dietary drinking water assessment (Tier 1 estimates) utilizes values generated by model and associated modeling parameters which are designed to provide conservative, health protective, high-end estimates of water concentrations.

- The residential exposure assessment utilizes: activity specific transfer coefficients and chemical-specific turf tranferable residue (TTR) studies for the post-application scenario. The refined residential assessment is based on reliable data and is unlikely to underestimate exposure/risk.

3.3 Dose Response Assessment

Discussion of Toxicological Endpoints:

Acute dietary endpoints: As there were no toxic effects attributable to a single dose, including the developmental toxicity studies, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. The changes in brain morphometrics seen in the developmental neurotoxicity study were not selected as they were observed only at a dose exceeding the Limit Dose (1442 mg/kg/day). Therefore, an acute RfD was not established for any population for BAS 510 F.

Chronic dietary endpoint: The HIARC selected the NOAEL of 21.8 mg/kg/day for establishing the chronic RfD based on the combined results of the following three studies: chronic rat, carcinogenicity rat and chronic dog. The HIARC noted that this NOAEL is higher than the NOAELs in the 90-day study in dogs (7.6 mg/kg/day), the two-generation reproduction study (10.1 mg/kg/day) and the developmental neurotoxicity study (14 mg/kg/day). However, these differences are due to an artifact of the dose selection process in these studies as shown below:

Study	NOAEL (mg/kg/day)	LOAEL (mg/kg/day)
90-day - dog	7.6	78.1
2-generation reproduction - rat	10.1	101.6
developmental neurotoxicity - rat	14.0	147

Because the gap between the NOAEL and LOAEL in these studies was large and the effects at the LOAELs were minimal (dog = increased alkaline phosphatase activity and hepatic weights; 2-

generation = decreased body weights and body weight gains in offspring; developmental neurotoxicity = decrease in pup body weight gains on post-natal days 1-4), the true no-observed-adverse-effect-level was probably considerably higher. Therefore, the selection of the NOAEL of 21.8 mg/kg/day from the 1-year dog study is conservative and appropriate for the overall risk assessments. In addition, the endpoints for risk assessment are based on thyroid effects seen in multiple species (mice, rats and dogs) and after various exposure durations (subchronic and chronic exposures) which were not observed at the LOAELs in either the two-generation reproduction or the developmental neurotoxicity studies.

Occupational/Residential endpoints: All of the incidental oral, dermal and inhalation endpoints are based on the chronic toxicity rat, carcinogenicity rat and 1-year dog studies. The HIARC noted that neither dermal nor systemic toxicity was seen at the Limit Dose (1000 mg/kg/day) in the 28-day dermal toxicity study in rats. The Committee, however, selected the oral NOAEL of 21.8 mg/kg/day because of the concerns for the decreases in the body weight and body weight gains seen in the offsprings in the two-generation reproduction and the developmental neurotoxicity studies. Additionally, this dose would address the concerns for thyroid and hepatotoxicity seen via the oral route in multiple species (mice, rats and dogs) after various exposure durations (90-day, 1-year and 2-years). There are no concerns that the effects will worsen following longer treatment.

For the dermal endpoints, a dermal study is available; however, the selected endpoint addresses potential effects on offspring, which are not normally examined in the dermal study. This endpoint is likely to be conservative because no systemic effects were observed in the dermal study up to the limit dose of 1000 mg/kg/day. In the reproduction study, the parental NOAEL is 112.6/1180.8 mg/kg/day based on decreases in body weight and body weight gain as well as hepatocyte degeneration in males only. No such effects were observed in the 28-day dermal study.

No repeated dose inhalation study was available. Because of this, the HIARC selected the oral NOAEL for this risk assessment. There are no concerns that the effects will worsen following longer treatment. Absorption via inhalation is assumed to be equivalent to absorption via the oral route. The lack of a repeated dose inhalation study is considered to be a data gap.

Table 4. Summary of Toxicological Dose and Endpoints for BAS 510 F			
Exposure Scenario	**Dose Used in Risk Assessment, UF**	**Special FQPA SF and Level of Concern for Risk Assessment**	**Study and Toxicological Effects**
Acute Dietary	No appropriate endpoint identified	NA	NA
Chronic Dietary (All populations)	NOAEL= 21.8 UF = 100 **Chronic RfD** = 0.218 mg/kg/day	FQPA SF = 1 **cPAD** = chronic RfD / FQPA SF = 0.218 mg/kg/day	Chronic rat, carcinogenicity rat and 1-year dog studies LOAEL = 57-58 mg/kg/day based on liver and thyroid effects
Incidental Oral (Short and intermediate term residential only)	NOAEL= 21.8 mg/kg/day	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	Chronic rat, carcinogenicity rat and 1-year dog studies LOAEL = 57-58 mg/kg/day based on liver and thyroid effects
Dermal (All Durations)	Oral study NOAEL=21.8 mg/kg/day (dermal absorption rate = 15%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	Chronic rat, carcinogenicity rat and 1-year dog studies LOAEL = 57-58 mg/kg/day based on liver and thyroid effects
Inhalation (All Durations)	Oral study NOAEL= 21.8 mg/kg/day (inhalation absorption rate = 100%)	**Residential** LOC for MOE = 100 **Occupational** LOC for MOE = 100	Chronic rat, carcinogenicity rat and 1-year dog studies LOAEL = 57-58 mg/kg/day based on liver and thyroid effects
Cancer (oral, dermal, inhalation)	**Classification: "Suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential."**		

UF = uncertainty factor, FQPA SF = Special FQPA safety factor, NOAEL = no observed adverse effect level, LOAEL = lowest observed adverse effect level, PAD = population adjusted dose (a = acute, c = chronic) RfD = reference dose, MOE = margin of exposure, LOC = level of concern, NA = Not Applicable

3.4 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disrupter Screening and Testing Advisory Committee (EDSTAC), EPA determined that there was scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disrupter Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, BAS 510 F may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

For BAS 510 F, the only effects which may indicate potential endocrine disruption were those involving the thyroid gland (weights and histopathology as well as increases/decreases of T_3, T_4 and TSH). The endpoint selections were based on these effects and therefore, will not under estimate these risks.

4.0 EXPOSURE ASSESSMENT

4.1 Summary of Registered and Proposed Uses

Registered Uses. None; BAS 510 F is a new fungicide ai and this is its first petition (1F06313).

Formulations. Two formulated end-use products are proposed for use on crops: a Wettable Granule (WG) termed BAS 510 02 F (Endura™ Fungicide; EPA Reg. No. 7969-ROT) containing 70% BAS 510 F and a WG termed BAS 516 02 F (Pristine™ Fungicide; EPA Reg. No. 7969-ROO) containing a 2:1 mixture of BAS 510 F and BAS 500 F (pyraclostrobin) as co-active ingredients (25.2%:12.8%). In addition, there is a 70 WG end-use product termed BAS 510 02 F Turf Fungicide (EPA Reg. No. 7969-ROA) proposed for use only on golf course turfgrass (nte 2.1 lbs ai/A/year). BAS 510 F is not currently planned for residential uses.

Proposed Uses on Crops. Endura™ is intended for use on beans, berries, bulb vegetables, canola, carrots, fruiting vegetables, grapes, lettuce, peanuts, pistachios, potatoes, stone fruit, strawberries, and tree nuts. Pristine™ is intended for use on berries, bulb vegetables, carrots, grapes, pistachios, stone fruit, strawberries, and tree nuts. Application is via multiple, foliar, broadcast sprays at a seasonal rate of ca 0.9-1.8 lbs ai/A, depending on crop and target disease. Typically, retreatment intervals are 1-3 weeks and minimum PHIs are 0-30 days. *Brassica* vegetables (subgroups 5A and 5B), cucurbit vegetables, mint, edible peas, certain root vegetables, and sunflower may also be treated with Endura™ or Pristine™, following use patterns based upon their submitted field trials.

Their use patterns are similar to those of the other crops listed above and are to be added to the applicable label(s).

Rotational Crops. Field accumulation studies indicate that detectable levels of indirect residues are expected in most crops planted after a 14-day interval into bare treated soil (1.8 lbs ai/A). Appropriate indirect residue tolerances are being proposed. The Endura™ and Pristine™ labels should include a 14-day plantback restriction for crops without registered uses.

4.2 Dietary Exposure/Risk Pathway

4.2.1 Residue Profile (Attachment 2, HED residue chemistry summary document of 08/15/03, M. Nelson, D278385, and Attachment 3, HED MARC decision memo of 01/09/03, M. Nelson, D286786)

Below are brief summaries from these documents:

Metabolism in Target Crops. Nature of the residue studies were conducted in grape (MRID 45405022), lettuce (MRID 45405021), and bean (MRID 45405023). No significant metabolism of BAS 510 F occurred in grapes or lettuce; unchanged parent was the only component identified, accounting for 92-98% and 99% TRR, respectively. In bean plants, BAS 510 F metabolized slowly; unchanged parent was the major component identified, accounting for up to 72% TRR in/on bean dry seeds and 99% TRR in/on bean plants; cleavage products 1-(chlorophenyl)-2-aminobenzene and 2-chloronicotinic acid were present in small amounts, accounting for <1% and <10% TRR, respectively. The MARC concluded that parent BAS 510 F is the sole residue of concern for risk assessment and the tolerance expression for primary (target) crops; the cleavage products were not included based on the limited cleavage which occurred and the low levels of their ingestion expected from dietary and environmental sources.

Metabolism in Rotational Crops. A confined rotational crop study (MRID 45405204) was conducted with three representative crops (radish, head lettuce, and wheat). In lettuce, radish (roots, tops), and wheat (forage,), parent BAS 510 F was the major residue identified (50-96% TRR), with the glucoside metabolite, M510F61 (see Attachment for name and structure), accounting for 1-21% TRR; only parent was identified in wheat grain. The MARC concluded (D286786) that parent BAS 510 F is the sole residue of concern for risk assessment and the tolerance expression for rotational (inadvertent or indirect residue) crops; M510F61 was not included based on its being found mainly in feed items and at a relatively low percentage compared to the parent.

Metabolism in Livestock. Nature of the residue studies were conducted in lactating goat (MRIDs 45405024 and 45405025) and laying hen (MRID 45405026). In both the goat and the hen, parent BAS 510 F, M510F 01 (hydroxy metabolite), and M510F 02 (M510F01 glucuronide) (see Attachment for names and structures) were identified as the major residues, with radioactivities ≥10% TRR; no amide bridge cleavage products were identified. Based on the structural similarity of BAS 510 F and M510F01, and the fact that the enzymatic hydrolysis step in the proposed enforcement method (DFG S19) will release M510F02 back to free M510F01, the MARC concluded that the combined residues of parent BAS 510 F, M510F 01, and M510F02 are the residues of

concern for risk assessment and the tolerance expression in livestock matrices. MARC decisions are summarized in **Table 5**, below.

Matrix	[illegible]	[illegible]
Target Crops	Parent	Parent
Rotational Crops	Parent	Parent
Livestock[2]	Parent, M510F01, M510F02	Parent, M510F01, M510F02
Water	Not Applicable	Parent

1 Both data collection and tolerance enforcement methods are available to measure these specific residues of concern in plant and livestock matrices (see §4.6-§4.10).

2 **In Livestock: The combined residues of BAS 510 F and its hydroxy metabolite, free (M510F01) and bound (M510F02), all expressed in parent equivalents.**

Data Collection Method for Plants. (Method D9908; MRID 45405027). This method determines residues of BAS 510 F (and, separately, also pyraclostrobin and its metabolite BF 500-3) in plant matrices. Residues are extracted with an aqueous organic solvent mixture followed by liquid/ liquid partitioning and column clean-up. Quantitation is by LC/MS/MS. This method has been adequately validated for data collections, and the reported limit of quantitation (LOQ) is 0.05 ppm for residues of BAS 510 F in/on plant matrices.

Data Collection Methods for Livestock. (Method 471/0; MRID 45405106 and Method476/0; MRID 45405105). Method 471/0 determines residues of BAS 510 F, M510F01, and M510F02 (as M510F01) in milk, eggs, and animal tissues/organs. Residues are extracted with methanol. The extract is treated with enzymes to deconjugate M510F02 to M510F01. Residues are isolated by liquid/liquid partitioning followed by column chromatography. Parent BAS 510 F and total M510F01 are quantitated by LC/MS/MS. The reported LOQ for each analyte is 0.01 ppm in milk and eggs and 0.025 ppm in other animal matrices. Method 476/0 was developed to determine nonextractable residues of BAS 510 F in liver and milk. The method is a common moiety method based on the quantification of metabolite M510F53 (see Attachment for name and structure). Residues are mixed with ACN:concentrated acetic acid and extracted by microwave, followed by liquid-liquid partitioning and column clean-up. Quantitation is by GC/MS using selected ion monitoring. This method has been adequately validated for data collections, and the reported LOQ is 0.01 ppm in milk and 0.05 ppm in liver.

Analytical Enforcement Method for Plants. (Method D0008; MRID 45405028). This method determines residues of BAS 510 F. Residues are extracted using an aqueous organic solvent mixture followed by liquid/liquid partitioning and column clean-up. Quantitation is by GC/MS using selected ion monitoring. The reported LOQ is 0.05 ppm for residues of BAS 510 F in plant matrices. The Analytical Chemistry Branch (ACB) in BEAD has concluded that this method is acceptable for

tolerance enforcement purposes in plant matrices without the need for an EPA validation (Agency memo of 08/12/03, D. Swineford and E. Kolbe, D284510). However, the method should state the type of inlet liner to be used (ACB recommends a minimum capacity of 700 µl).

Analytical Enforcement Method for Livestock. (Method DFG S19; MRID 45405103). This method determines residues of BAS 510 F, M510F01, and M510F02 (as M510F01). Residues are extracted with methanol. The extract is treated with enzymes to release M510F02 to free M510F01. Residues are isolated by liquid/liquid partition followed by column chromatography. Total M510F01 is acetylated followed by a column clean-up. Parent BAS 510 F and acetylated M510F01 are quantitated by GC/ECD (electron capture). The reported LOQ for each analyte is 0.01 ppm in milk and 0.025 ppm in other animal matrices. ACB/BEAD has conducted a successful tolerance method validation on this method using beef liver (Agency memo of 07/17/03, D. Swineford and E. Kolbe, D284440). ACB/BEAD recommended that this method be considered acceptable for tolerance enforcement purposes in livestock matrices.

Multiresidue Methods Testing. Residues of BAS 510 F and its hydroxy metabolite M510F01 had good responses with GC/ECD on a DB-1 column under Protocol C. Neither analyte was recovered at ≥30% using Protocols D, E, and F. Protocol A was not applicable. Protocol B was not applicable for BAS 510 F and yielded inconsistent recoveries of M510F01.

Freezer Storage Stability in Plant Commodities. Submitted freezer storage stability data (MRID 45405109) indicate that residues of BAS 510 F are stable in diverse representative crop matrices (sugar beet root, cabbage, canola seed, pea, peach, and wheat grain, forage, and straw) for up to approximately 1 year (ongoing study) of frozen storage. BAS 510 F residues have also been shown (MRID 45405122) to be stable in peanut oil and meal for up to 45 days (duration of study). These data support the freezer storage interval (from collection-to-analysis) of samples in the various crop field trial, field accumulation, and processing studies (except grape and tomato). Freezer storage stability data are being requested for grape juice (MRID 45405125) and tomato paste (MRID 45405126).

Freezer Storage Stability in Livestock Commodities. Submitted freezer storage stability data for cattle (MRID 45405108) and poultry (MRID 45643801) matrices indicate that residues of BAS 510 F and its hydroxy metabolite M510F01 are stable for up to 5.5 months (duration of study) in cow milk, liver, and muscle (only matrices tested) and 2.6 months (duration of study) in eggs. These data support the freezer storage interval (from collection-to-analysis) of samples in the cattle and poultry feeding studies.

Magnitude of the Residue in Target Crops. Field trials were conducted to determine the magnitude of BAS 510 F residues in the following crops: almonds, berries (blueberry and raspberry), *Brassica* vegetables (broccoli, cabbage, mustard greens), canola seed, carrot, cucurbit vegetables (cucumber, cantaloupe, and summer squash), grape, legume vegetables (except soybeans), lettuce (head and leaf), mint, onion (dry bulb and green), peanut, pecan, pepper (bell and chili), pistachio, potato, radish (roots and tops) stone fruit (cherry, peach, plum), strawberry, sunflower seed, and tomato. These trials were conducted in the United States and Canada in the required Regions, using the maximum label rate and number of applications, and the minimum retreatment

interval and PHI for each crop or crop group. Based on these trials, appropriate direct use tolerances (ranging from 0.05 to 30.0 ppm) are recommended below.

Table 6. Use Pattern from Label Directions [and Crop Field Trials][1] for BAS 510 F Co-Active Ingredient in BAS 516 F [Pristine™] Fungicide

Crop	Max Field Appl Rate (lb ai/A)	Max Label Proposed Use Rate (lb ai/A)	Field Trial PHI (days)	Label proposed PHI (days)	Max Residues From Field Trials (ppm)	Recommended Tolerances (ppm)
Carrot	[1.02-1.07]	0.99	[0]	0	[0.381]	0.7
Bulb Vegetables (Crop Group 3)	[1.79-1.83]	1.75	[7]	7	[2.94]	3.0
Stone Fruit (Crop Group 12)	[1.14-1.17]	0.92-1.15	[0]	0	[1.64]	1.7
Berries (Crop Group 13)	[1.48-1.52]	0.72-1.44	[0]	0	[3.31]	3.5
Tree Nuts (Crop Group 14)	[0.90-0.93]	0.69-0.91	[14-148]	14[2]	meat [0.20] almond hulls [2.81]	meat 0.70 almond hulls 3.0
Pistachio	[0.92-0.93]	0.91	[14-15]	14	[0.64]	0.70
Grape	[1.06-1.12]	1.09	[14]	14	[3.10]	3.5
Strawberry	[1.81-1.89]	1.81	[0-1]	0	[1.16]	1.2

[1] Actual parameters utilized during crop field trials are shown in brackets.
[2] For almonds, minimum PHI is five (5) weeks after petal fall.

Table 7. Use Pattern from Label Directions [and Crop Field Trials][1] for BAS 510 F [Endura™] Fungicide

Crop	Max Field Appl Rate (lb ai/A)	Max Label Proposed Use Rate (lb ai/A)	Field Trial PHI (days)	Label proposed PHI (days)	Max Residues From Field Trials (ppm)	Recommended Tolerances (ppm)
Carrot[2]	[1.02-1.07]	0.98	[0]	0	[0.381]	0.7
Tuberous and Corm Vegetables (Crop Group 1C)	[0.87-0.92]	0.90	[29-30]	30	[<0.05]	0.05
Bulb Vegetables[2] (Crop Group 3)	[1.79-1.83]	1.78	[7]	7	[2.94]	3.0
Lettuce	[0.98-1.02]	0.96	[13-15]	14	leaf [10.4]; head [6.2]	leaf 11 head 6.5
Legume Vegetables - Beans (Crop Group 6)	[0.97-1.05]	0.96	[7,21]	7,21	[2.35]	Subgroup 6A: 1.6 Subgroup 6B: 0.6 Subgroup 6C: 2.5
Fruiting Vegetables[2] (Crop Group 8)	[0.89-1.12]	1.09	[0]	0	[0.99]	1.2
Stone Fruit[2] (Crop Group 12)	[1.14-1.17]	0.93-1.15	[0]	0	[1.64]	1.7
Berries[2] (Crop Group 13)	[1.48-1.52]	0.70-1.40	[0]	0	[3.31]	3.5

Table 7. Use Pattern from Label Directions [and Crop Field Trials][1] for BAS 510 F [Endura™] Fungicide

Crop	Max Field Appl Rate (lb ai/A)	Max Label Proposed Use Rate (lb ai/A)	Field Trial PHI (days)	Label proposed PHI (days)	Max Residues From Field Trials (ppm)	Recommended Tolerances (ppm)
Tree Nuts[2] (Crop Group 14)	[0.90-0.93]	0.70-0.93	[14-148]	14[3]	meat [0.20]; almond hull, [2.81]	meat 0.70 almond hull, 3.0
Pistachio[2]	[0.92-0.93]	0.93	[14-15]	14	[0.64]	0.70
Grape[2]	[1.06-1.12]	1.09	[14]	14	[3.10]	3.5
Strawberry[2]	[1.81-1.89]	1.75	[0-1]	0	[1.16]	1.2
Peanut	[1.25-1.38]	1.31	[13-15]	14	[0.054]	0.05
Canola[4]	[0.75-0.82]	0.52	[19-23]	21	[3.42]	3.5

[1] Actual parameters utilized during crop field trials are shown in brackets.
[2] The 70% BAS510F (nicobifen) formulation utilized at field trials for these crops was applied to the treated plots in combination with another experimental active ingredient, BAS500F (pyraclostrobin), as part of a tank-mix.
[3] For almonds, minimum PHI is five (5) weeks after petal fall.
[4] The 70% BAS510F (nicobifen) formulation utilized at field trials for canola was applied to the treated plots in combination with another experimental active ingredient, BAS505F(pyraclostrobin), as part of a tank-mix.

Magnitude of the Residue in Rotational Crops. Tier III extended field rotational crop studies resulted in detectable residues in a variety of crops planted into bare soil 14 days following the last of 3 applications totaling 1.8 lbs BAS 510 F ai/A. Appropriate indirect residue tolerances (ranging from 0.05 to 8.0 ppm) are being proposed .

Table 8. Use Patterns from Crop Field Trials[1] Conducted on Those "Rotational Crops" Which Qualify for Direct Uses and Target Crop Tolerances. These Crops/Use Patterns Should be Added to the Endura™ and/or Pristine™ Labels, as Applicable.

Crop	Max Field Appl Rate (lb ai/A)	Max Label Proposed Use Rate (lb ai/A)	PHI (days)	[Max Residue] (ppm)	Recommended Tolerance
Brassica "Cole" Leafy Vegetables (Crop Group 5)[1]	[0.78-0.83]	0.80	0 (5A) 14 (5B)	[2.82][2] CSG-5A [15.4][2] CSG-5B	3.0 18.0
Cucurbits (Crop Group 9)[3]	[1.20-1.23]	1.20	0	CG-9 except cuke [1.48][4] cuke [0.16]	CG-9 except cuke 1.6 cuke 0.2
Edible Peas (Dried, Succulent & Edible Pod)	[0.99-1.03]	1.0	6-8[5] 20-22	CG-6 except soybean [1.53]	Subgroup 6A: 1.6 Subgroup 6B: 0.6 Subgroup 6C: 2.5
Mint	[1.59-1.61]	1.60	14-15	[28.6]	30.0
Root Vegetable (except sugar beet, garden beet, radish, and turnip)	[1.02-1.07]	1.02	0	[0.61]	0.7

Table 8. Use Patterns from Crop Field Trials[1] Conducted on Those "Rotational Crops" Which Qualify for Direct Uses and Target Crop Tolerances. These Crops/Use Patterns Should be Added to the Endura™ and/or Pristine™ Labels, as Applicable.

Crop	Max Field Appl Rate (lb ai/A)	Max Label Proposed Use Rate (lb ai/A)	PHI (days)	[Max Residue] (ppm)	Recommended Tolerance
Sunflower Seed	[0.79-0.80]	0.80	20-21	[0.54]	0.60

[1] Includes broccoli, cabbage and mustard greens; use pattern was the same for all three.
[2] Max residues: mustard greens = 15.4 ppm (14d PHI), cabbage = 2.82 ppm (0d PHI), broccoli = 2.73 ppm (0d PHI) (>5X spread, so CG-5 tolerance inappropriate; CSG-5A & CSG-5B tolerances appropriate).
[3] Includes cantaloupe, cucumber and summer squash; use pattern was the same for all three.

[4] Max residues: cantaloupe = 1.48 ppm, squash = 1.08 ppm , cucumber = 0.16 ppm (>5X spread, so CG-9, tolerances inappropriate).
[5]PHI was 6 to 8 days for succulent peas (shelled & edible podded) and 20 to 22 days for dried shelled peas.

Magnitude of the Residue in Processed Food/Feed. Processing studies were conducted on canola seed, grape, mint, peanut, plum, rice grain, soybean seed, sunflower seed, tomato, and wheat grain to determine concentration factors during normal processing of the raw agricultural commodity. Based on NDR (<0.05 ppm) in alfalfa seed, cotton seed, and potatoes, processing studies were not required for those commodities. Concentration of residues occurred in canola oil, peanut oil and meal, raisins, rice hulls, and soybean hulls and appropriate tolerances (ranging from 0.15 to 8.5 ppm) are being proposed.

Magnitude of the Residue in Livestock. Cattle (MRID 45405110) and poultry (MRID 45643801) feeding studies were conducted. Lactating dairy cows ate BAS 510 F-laced feed for 29-30 days at levels equivalent to 1.8, 5.9, and 20.2 ppm in the diet. Laying hens were dosed daily via balling gun with encapsulated BAS 510 F for 29 days at levels equivalent to 1.0, 5.3, and 19.6 ppm in the diet. Based on the residue data from these studies, the proposed crop tolerances (target and rotational), and calculations of maximum theoretical dietary burdens to livestock using "worst case" diets, appropriate animal commodity tolerances (ranging from 0.02 to 0.35 ppm) are being proposed.

International Harmonization. BAS 510 F is a new fungicide. There are currently no pending or established Codex maximum residue limits (MRLs) for BAS 510 F, and no established Canadian or Mexican MRLs either. The US EPA and PMRA/Canada are jointly reviewing this subject petition (1F06313), and the forthcoming tolerances are being harmonized with respect to the residue of concern and tolerance levels.

4.2.2 Chronic Dietary Exposure and Risk. (Attachment 4, HED DEEM memo of 05/29/03, M. Doherty, D289724)

cPAD = chronic RfD = 0.218 mg/kg bwt/day.
BAS 510 F chronic dietary exposure assessments were conducted using the Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID™, Version 1.3), which incorporates consumption data from USDA's Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported

consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the cPAD. This procedure is performed for each population subgroup.

This assessment used tolerance-level residue values for all of the commodities associated with PP# 1F06313 for which HED determined that tolerances are necessary, as well as estimated tolerance levels for commodities associated with PP# 2F06434. In a few cases residue levels higher than the final tolerances were used due to lowering of some tolerances to harmonize with Canadian MRL's subsequent to the dietary risk assessment. Tolerances are based on field trials, rotational crop studies, and livestock feeding studies. In target and rotational crops, the residue of concern for both the tolerance expression and risk assessment is parent BAS 510 F, *per se*. In livestock, the residues of concern for both the tolerance expression and risk assessment are the combined residues of BAS 510 F and the metabolites M510F01 and M510F02. One hundred percent crop treated was assumed for all commodities in this assessment. Empirical processing factors were used for all commodities except processed potato, peanut butter, and all dried foods (meat, potato, fruits, etc.) except prunes and raisins. Since empirical factors were not provided for those foods, the default factors from DEEM version 7.76 were used.

Field trials for PP# 2F06434 have not yet been reviewed by the Agency. For those commodities (pome fruits and hops), the petitioner has requested tolerance levels of 3.0 ppm and 35 ppm, respectively. HED has used the requested tolerance level of 35 ppm for hops. However, due to uncertainty regarding the proposed use pattern and the submitted residue data summary, we have used 5 ppm, rather than 3 ppm, in this assessment to ensure that we do not underestimate dietary exposure to BAS 510 F.

The analysis is summarized in Table 9. Even with these highly conservative assumptions, the risk estimates are well below HED's level of concern. Estimated exposures are less than 0.077 mg/kg/day (35% of the cPAD) for all population subgroups.

Table 9. Results of Chronic Dietary Exposure Analysis			
Population Subgroup	cPAD (mg/kg/day)	Exposure (mg/kg/day)	% cPAD
General U.S. Population	0.218	0.017494	8
All Infants (< 1 year old)	0.218	0.051445	24
Children 1-2 years old	0.218	0.076537	35
Children 3-5 years old	0.218	0.050909	23
Children 6-12 years old	0.218	0.023339	11
Youth 13-19 years old	0.218	0.011947	6
Adults 20-49 years old	0.218	0.011515	5
Adults 50+ years old	0.218	0.012424	6
Females 13-49 years old	0.218	0.011657	5

4.2.3 Cancer Dietary

The Cancer Assessment Review Committee (CARC) classified BAS 510 F as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", and, therefore, the quantification of human cancer risk is not recommended.

4.3 Water Exposure/Risk Pathway (Attachment 5, EFED memo of 09/16/02, C. Sutton, D278418)

EFED provided the Tier I estimated environmental concentrations (EECs) for BAS 510 F in surface water and in groundwater for use in the human health risk assessments. The EECs are summarized in Table 1. EFED used the simulation model FIRST to calculate the surface water EECs and used the simulation model SCI-GROW to calculate the groundwater EEC. Because BAS 510 F is a new chemical, monitoring data were not available.

For the surface water and groundwater assessments, the application rate for turf was used, which represents the highest seasonal application rate (i.e., 2.1 lb a.i./A/season or 0.350 lb a.i./A/application applied six times at 14-day intervals) on the proposed labels. It is noted that the highest single application rate (0.547 lb a.i./A), associated with the use of the pesticide on fruiting vegetables, did not result in EEC values higher than those reported below (since the proposed total seasonal application rate for fruiting vegetables is only 1.1 lb a.i./A/season).

In response to concerns raised by the MARC committee, an attempt was made to assess the potential for two possible degradates, 2-(4-chlorophenyl)aniline and 2-chloro pyridine, to reach drinking water sources. No data were submitted by the registrant on the mobility or persistence of either of the two compounds. However, it is noted that the degradates were not isolated in any of the submitted laboratory or field studies. The possible degradate 2-(4-chlorophenyl)aniline was monitored in an aerobic soil metabolism study and was not detected in any of the samples. The possible degradate 2-chloro pyridine, which could form from the degradation of 2-chloronicotinic acid, was not monitored specifically in the studies. However, the acceptable material balances in the laboratory metabolism studies indicated that if the degradate was present in the unidentified fraction, it was not present in

significant quantities. It is likely that if the compound was formed, it was present in the soil samples as a bound residue. The registrant submitted additional information, in the form of published literature, on the transformation of chlorinated pyridines. Based on the published literature and the results of laboratory studies, the registrant concluded that the metabolic products of 2-chloronicotinic acid were carbon dioxide and bound residues. MARC concluded that parent only is needed to be included in the drinking water assessment.

Surface water drinking water sources	acute: 87.0 ug/L (ppb) chronic: 25.6 ug/L
Groundwater drinking water sources	0.571 ug/L (ppb) or 571 ng/L (parts per trillion)

4.4 Non-Occupational Exposure/Risk Pathway (Attachment 6, HED ORE memo of 06/23/03, Shih-Chi Wang, D290072)

The Agency uses the term "post-application" to describe exposures to individuals that occur as a result of being in an environment that has been previously treated with a pesticide. There are two recreational scenarios associated with BAS 510 F that could lead to exposures for adults and children: 1.) golfing and 2.) picking their own fruit. These exposure durations are anticipated to be short-term. Because "U-pick" is a "one-time" event (duration<1-day) and the HIARC found that the oral studies indicated there were no endpoints appropriate to quantitate acute risk. "U-pick" exposure/risk was not evaluated. Therefore, only golfing scenario is evaluated in this assessment with respect to non-occupational exposures.

The BAS 510 02F label specifies that this product is intended for golf course use only, and not for use on residential turfgrass or turfgrass being grown for sale or other commercial use such as sod production. Although the label does not indicate that the product is applied by licenced or commercial applicators, it is acknowledged that the homeowner will not be applying the product to golf courses. Therefore, a risk assessment for homeowner handler exposure is not required.

The Registrant, BASF Corporation submitted a turf transferable residue (TTR) study and four dislodgeable residue (DFR) studies using BAS 510 F in support of this registration action. The Health Canada Pest Management Regulatory Agency (PMRA) performed primary reviews on the studies and HED performed secondary review. HED concurred with the DFR study reviews done by PMRA.

The non-occupational dermal post-application exposure and risk was calculated by coupling chemical specific TTR values with activity specific transfer coefficient (Tc) values from the HED Science Advisory Council For Exposure Policy Number 3.1: Agricultural Transfer Coefficients, August 2000.

The TTR study provided two residue values, both from the Pennsylvania site, which were selected to estimate high end exposure from turf. The highest turf average daily residue value (0.1313 ug/cm2) was collected from a sampling site when the turf was wet which resulted in higher than normal transferable residues. The lower turf residue value (0.048 ug/cm2) was collected when the turf was

dry and resulted in lower transferable residues. It should be noted that the Tc used to estimate dermal exposure to turf is based on samples collected on dry surfaces. However, golf courses are often automatically sprayed by built in sprinkler systems in the morning. Therefore, HED thought it was appropriate to assess dermal exposure in both dry and wet conditions. Furthermore, TTR values were normalized (adjusted) to the maximum label application rate.

Table 11 provides a summary of dermal post-application exposure for adults golfing. The highest daily dose from golf turf exposure is 0.0008 mg/kg/day (. Dermal post-application exposure MOEs for adults and children were all greater than the target MOE of 100 and therefore did not exceed HED's level of concern. Although specific MOE's were not calculated for youths playing golf, the adult MOE's are considered representative since the body surface area to weight ratios for adolescents do not vary significantly from those for adults. There is the potential for oral exposure due to hand-to-mouth transfer of pesticide residues from picking your own fruit. However, HED does not have an applicable database for estimating consumption of U-Pick fruits in the field or hand-to-mouth activity during fruit picking. In addition, HIARC did not select an acute dietary endpoint that would be appropriate for this type of exposure. The dietary exposure assessment /DEEM will address exposure due to ingestion.

BAS 510 02F Turf Fungicide TTR Study MRID# 45405301	0.069[a]	0.001	500	4	15	70	0.000295	74000
	0.188[b]						0.0008	27000

1a. The highest daily average Transferable Turf Residue for dry turf resulting from Pennsylvania TTR study data (Adjusted for difference in application rate from 0.35 to .5 lb ai/A max rate)
1b. The highest daily average Transferable Turf Residue for wet turf resulting from Pennsylvania TTR study data (Adjusted for difference in application rate from 0.35 to .5 lb ai/A max rate)
2. DD (mg/kg/day) = DFR x CF1 x Tc x ET x %DA/BW
3. Dermal MOE = NOAEL (21.8 mg/kg/day)/ Daily Dose (mg/kg/day)

4.5 Other (Spray Drift, etc.)

Spray drift is always a potential source of exposure to residents nearby to spraying operations. This is particularly the case with aerial application, but, to a lesser extent, could also be a potential source of exposure from the ground application method employed for BAS 510 F. The Agency has been working with the Spray Drift Task Force, EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices. The Agency is now requiring interim mitigation measures for aerial applications that must be placed on product labels/labeling. The Agency has completed its evaluation of the new data base submitted by the Spray Drift Task Force, a membership of U.S. pesticide registrants, and is developing a policy on how to appropriately apply the data and the AgDRIFT computer model to its risk assessments for pesticides applied by air, orchard airblast and ground hydraulic methods. After the policy is in place, the Agency may impose further refinements in spray drift management practices to reduce off-target drift and risks associated with aerial as well as other application types where appropriate.

5.0 AGGREGATE RISK ASSESSMENT AND RISK CHARACTERIZATION

Aggregate exposure risk assessments were performed for short- term (food + drinking water + residential) and chronic aggregate exposure (food + drinking water). Since HED does not have ground and surface water monitoring data to calculate a quantitative aggregate exposure, drinking water levels of comparison (DWLOCs) were calculated. A DWLOC is a theoretical upper limit on a pesticide's concentration in drinking water in light of total aggregate exposure to a pesticide in food, drinking water, and through residential uses. A DWLOC will vary depending on the toxic endpoint, drinking water consumption, body weights, and pesticide uses. Different populations will have different DWLOCs. HED uses DWLOCs in the risk assessment process to assess potential concern for exposure associated with pesticides in drinking water. DWLOC values are not regulatory standards for drinking water.

To calculate chronic DWLOCs, the dietary food estimates (from DEEM™) were subtracted from the chronic PAD value to obtain the maximum water exposure level. DWLOCs were then calculated using the standard body weights and drinking water consumption figures: 70kg/2L (adult male and US Population), 60 kg/2L (adult female), and 10kg/1L (infant & children).

5.1 Acute Risk

As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk to the general population or to the subpopulation females 13-50 years old. Therefore, there is no acute reference dose (aRfD) or acute population-adjusted dose (aPAD) for the general population or females 13-50 years old. An acute aggregate risk assessment is not needed.

5.2 Short-Term Risk

The short-term aggregate risk assessment takes into account average exposures estimates from dietary consumption of BAS 510 F (food and drinking water) and non-occupational uses (golf course). Postapplication exposures from the proposed use on golf course is considered short- term (see Section 4.4), and applies to adults and youth. Therefore, a short-term aggregate risk assessment was conducted. Since all endpoints are from the same study, exposures from different routes can be aggregated. Table 12 summarizes the results. The MOE from food and non-occupational uses is 1200, and the calculated short- term DWLOC is 6000 ppb. Compared to EFED's surface and ground water EECs, the DWLOC is considerably greater and therefore, short- term aggregate risk does not exceed HED's level of concern.

The MOE and DWLOC are also considered representative for youth for the reason stated in Section 4.4 (i.e., similar body surface area to weight ratios) plus the dietary exposure for youth (13-19 years old) being less than the general U.S. population.

Table 12. Short-Term Aggregate Risk and DWLOC Calculations (Inhalation/Oral/Dermal Endpoints and NOAELs the Same)										
Population	*Short or Intermediate*-Term Scenario									
	NOAEL mg/kg/day	Target MOE[1]	Max Exposure[2] mg/kg/day	Average Food Exposure mg/kg/day	Residential Exposure[3] mg/kg/day	Aggregate MOE (food and residential)[4]	Max Water Exposure[5] mg/kg/day	Ground Water EEC[6] (*units*)	Surface Water EEC[6] (*units*)	Short-Term DWLOC[7] (µg/L)
General U.S. pop[8]	21.8	100	0.218	0.017494	0.0008	1200	0.199706	0.571	25.60	6000

[1]The target MOE for dermal is 100.

[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE

[3] Residential Exposure = Dermal exposure from golf course only

[4] Aggregate MOE = [NOAEL ÷ (Avg Food Exposure + Residential Exposure)]

[5] Maximum Water Exposure (mg/kg/day) = Target Maximum Exposure - (Food Exposure + Residential Exposure)

[6] The crop producing the highest level was used.

[7] $DWLOC(\mu g/L) = \frac{[\text{maximum water exposure (mg/kg/day) x body weight (kg)}]}{[\text{water consumption (L) x } 10^{-3} \text{ mg/µg}]}$

[8] Adult female body weight was used, which covers adult male risk. The dietary exposure for the U. S. population is higher than that of groups having residential (golf) exposure (i.e., adults, youth 13-19).

5.3 Chronic Risk

The chronic aggregate risk assessment takes into account average exposures estimates from dietary consumption of BAS 510 F (food and drinking water) and residential uses. Since the exposure from turf grass (golf course) is considered short term (see Section 4.4), the chronic aggregate assessment included food and drinking water only. The calculated chronic DWLOCs for chronic exposure to BAS 510 in drinking water range from 1400 to 7000 µg/L (ppb). EECs generated by EFED are less than HED's calculated chronic DWLOCs (Table 13). Therefore, the chronic aggregate risk associated with the proposed use of BAS 510 does not exceed HED's level of concern for the general U.S. population or any population subgroups.

Table 13. Chronic Aggregate Exposures to BAS 510 Residues.

Scenario/ Population Subgroup	cPAD, (mg/kg/day)	Chronic Food Exposure, (mg/kg/day)	Maximum Chronic Water Exposure[1], (mg/kg/day)	Ground Water EEC[2], (ppb)	Surface Water EEC[2], (ppb)	Chronic DWLOC[3], (ppb)
General U.S. Population	0.218	0.017494	0.200506	0.571	25.6	7000
All Infants (< 1 year old)	0.218	0.051445	0.166555	0.571	25.6	1700
Children 1-2 years old	0.218	0.076537	0.141463	0.571	25.6	1400
Females 13-49 years old	0.218	0.011657	0.206343	0.571	25.6	6200
Adults 50+ years old	0.218	0.012424	0.205576	0.571	25.6	7200

1 Maximum chronic water exposure (mg/kg/day) = cPAD (mg/kg/day) - chronic food exposure from DEEM (mg/kg/day).

2 EECs from EFED studies.

3 Chronic DWLOCs were calculated as follows:

$$\text{Chronic DWLOC}(\mu g/L) = \frac{[\text{maximum chronic water exposure (mg/kg/day) x body weight (kg)}]}{[\text{water consumption (L) x } 10^{-3}\ \text{mg}/\mu g]}$$

5.4 Cancer Risk

The Cancer Assessment Review Committee (CARC) classified BAS 510 F as, "suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential", and, therefore, the quantification of human cancer risk is not recommended. In accordance with the EPA draft cancer risk assessment guidelines of July, 1999, the CARC classified BAS 510 F in the above category based on the following weight of evidence considerations:

1. In male Wistar rats, there was a significant trend (but not pairwise comparison) for the combined thyroid adenomas and carcinomas. This trend was driven by the increase in adenomas.

2. In the female rats, there was only a borderline significant trend for thyroid adenomas (there were no carcinomas).

3. The mouse study was negative as were all of the mutagenic tests.

Consistent with this weak evidence of carcinogenic effects, the CARC indicated that a dose-response assessment for cancer (either linear low-dose extrapolation or margin of exposure calculation) was not needed.

6.0 CUMULATIVE RISK

FQPA (1996) stipulates that when determining the safety of a pesticide chemical, EPA shall base its assessment of the risk posed by the chemical on, among other things, available information concerning the cumulative effects to human health that may result from dietary, residential, or other non-occupational exposure to other substances that have a common mechanism of toxicity. The reason for consideration of other substances is due to the possibility that low-level exposures to multiple chemical substances that cause a common toxic effect by a common mechanism could lead to the same adverse health effect as would a higher level of exposure to any of the other substances individually. A person exposed to a pesticide at a level that is considered safe may in fact experience harm if that person is also exposed to other substances that cause a common toxic effect by a mechanism common with that of the subject pesticide, even if the individual exposure levels to the other substances are also considered safe.

HED did not perform a cumulative risk assessment as part of this tolerance action for BAS 510 because HED has not yet initiated a review to determine if there are any other chemical substances that have a mechanism of toxicity common with that of BAS 510. For purposes of this tolerance action, EPA has assumed that BAS 510 does not have a common mechanism of toxicity with other substances.

On this basis, the Registrant must submit, upon EPA's request and according to a schedule determined by the Agency, such information as the Agency directs to be submitted in order to evaluate issues related to whether BAS 510 shares a common mechanism of toxicity with any other substance and, if so, whether any tolerances for BAS 510 need to be modified or revoked. If HED identifies other substances that share a common mechanism of toxicity with BAS 510, HED will perform aggregate exposure assessments on each chemical, and will begin to conduct a cumulative risk assessment.

HED has recently developed a framework that it proposes to use for conducting cumulative risk assessments on substances that have a common mechanism of toxicity. This guidance was issued for public comment on January 16, 2002 (67 FR 2210-2214) and is available from the OPP Website at: http://www.epa.gov/pesticides/trac/science/cumulative_guidance.pdf. In the guidance, it is stated that a cumulative risk assessment of substances that cause a common toxic effect by a common mechanism will not be conducted until an aggregate exposure assessment of each substance has been completed.

Before undertaking a cumulative risk assessment, HED will follow procedures for identifying chemicals that have a common mechanism of toxicity as set forth in the "*Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity*" (64 FR 5795-5796, February 5, 1999).

7.0 OCCUPATIONAL EXPOSURE AND RISK (Attachment 6, HED ORE memo of 06/23/03, Shih-Chi Wang, D290072)

Pesticide handler and workers performing post-application activities will be exposed to BAS 510 F during and after the application of the fungicide. No data on the number of exposure days per year was provided. For this risk assessment, it was assumed that handlers would be exposed for less than 6 months per year. Long-term exposure is not expected. For detailed use rates and use patterns, please see Attachment 6.

7.1 Occupational Handler

All MOEs for the handlers performing agricultural crop uses were greater than the target of 100 at the baseline level (ranging from 460 to 31,000). All MOEs for the handlers performing golf course turfgrass uses were also greater than the target of 100 at the baseline level (ranging from 7,300 to 27,000). Summaries of the risks for handlers are presented in Table 14

Table 14. Non-Cancer (Short- and Intermediate- Term) Risk for BAS 510 F Handlers.

Exposure Scenario (Scenario #)	Mitigation Level[a]	Dermal Unit Exposure[b] (mg/lb ai)	Inhalation Unit Exposure[c] (ug/lb ai)	Crop	Application Rate (lb ai/A)	Amount Treated[d] (A/day)	Daily Dermal Dose[e] (mg/kg/day)	Daily Inhalation Dose[f] (mg/kg/day)	Combined Daily Dose[g] (mg/kg/day)	MOE[h]
Dry Flowables for Ground-boom application (1)	Baseline	0.066	0.77	Carrots	0.20	80	0.0023	0.0002	0.0025	8,700
				Bulb Vegs, Cucurbits	0.30		0.0034	0.0003	0.0037	5,900
				Root Vegs	0.34		0.0039	0.0003	0.0042	5,200
				Sm. Berries, Grapes, Strawberries	0.35		0.0040	0.0003	0.0043	5,100
				Brassica Leafy Vegs., Mint	0.40		0.0045	0.0004	0.0049	4,500
				Peanuts, Potatoes	0.44		0.0050	0.0004	0.0054	4,000
				Dry/Succul. Beans, Lettuce	0.48		0.0054	0.0004	0.0058	3,800
				Edible Peas	0.50		0.0057	0.0004	0.0061	3,600
				Turfgrass		40	0.0028	0.0002	0.0030	7,300
				Fruit. Vegs	0.55	80	0.0062	0.0005	0.0067	3,300
				Canola	0.26	200	0.0074	0.0006	0.0080	2,700
				Sunflower	0.40		0.0113	0.0009	0.0122	1,800
Dry Flowables for Air Blast application (2)	Baseline	0.066	0.77	Stone Fruits, Tree Nuts, Pistachio	0.23	40	0.0013	0.0001	0.0014	15,600
Dry Flowables for Aerial application (3)	Baseline	0.066	0.77	Carrots	0.20	350	0.0099	0.0008	0.0107	2,000
				Stone Fruits, Tree Nuts, Pistachio	0.23		0.0114	0.0009	0.0123	1,800
				Bulb Veg.	0.30		0.0149	0.0012	0.0161	1,400

Exposure Scenario (Scenario #)	Mitigation Level[a]	Dermal Unit Exposure[b] (mg/lb ai)	Inhalation Unit Exposure[c] (ug/lb ai)	Crop	Application Rate (lb ai/A)	Amount Treated[d] (A/day)	Daily Dermal Dose[e] (mg/kg/day)	Daily Inhalation Dose[f] (mg/kg/day)	Combined Daily Dose[g] (mg/kg/day)	MOE[h]
				Sm. Berries, Grapes, Strawberries	0.35		0.0173	0.0014	0.0187	1,200
				Peanuts, Potatoes	0.44		0.0218	0.0017	0.0235	930
				Dry/Succul. Beans, Lettuce	0.48		0.0238	0.0019	0.0257	850
				Fruit. Vegs	0.55		0.0272	0.0021	0.0293	740
				Canola	0.26	1,200	0.0441	0.0034	0.0475	460
Sprays with Ground-boom (4)	Baseline	0.014	0.74	Carrots	0.20	80	0.0005	0.0002	0.0007	31,000
				Bulb Vegs, Cucurbits	0.30		0.0007	0.0003	0.0010	22,000
				Root Vegs	0.34		0.0008	0.0003	0.0011	20,000
				Sm. Berries, Grapes, Strawberries	0.35		0.0008	0.0003	0.0011	20,000
				Brassica Leafy Vegs., Mint	0.40		0.0010	0.0003	0.0013	17,000
				Peanuts, Potatoes	0.44		0.0011	0.0004	0.0015	15,000
				Dry/Succul. Beans, Lettuce	0.48		0.0012	0.0004	0.0016	14,000
				Edible Peas	0.50		0.0012	0.0004	0.0016	14,000
				Turfgrass		40	0.0006	0.0002	0.0008	27,000
				Fruit. Vegs	0.55	80	0.0013	0.0005	0.0018	12,000
				Canola	0.26	200	0.0016	0.0006	0.0022	9,900
				Sunflower	0.40		0.0024	0.0008	0.0032	6,800

Exposure Scenario (Scenario #)	Mitigation Level[a]	Dermal Unit Exposure[b] (mg/lb ai)	Inhalation Unit Exposure[c] (ug/lb ai)	Crop	Application Rate (lb ai/A)	Amount Treated[d] (A/day)	Daily Dermal Dose[e] (mg/kg/day)	Daily Inhalation Dose[f] (mg/kg/day)	Combined Daily Dose[g] (mg/kg/day)	MOE[h]
Sprays with Air Blast (5)	Baseline	0.36	4.5	Stone Fruits, Tree Nuts, Pistachio	0.23	40	0.0071	0.0006	0.0077	2,800
Sprays with fixed wing Aircraft (6)	Engineer. Control	0.0050	0.068	Carrots	0.20	350	0.0008	0.0001	0.0009	24,000
				Stone Fruits, Tree Nuts, Pistachio	0.23		0.0009	0.0001	0.0010	21,800
				Bulb Veg.	0.30		0.0011	0.0001	0.0012	18,000
				Sm. Berries, Grapes, Strawberries	0.35		0.0013	0.0001	0.0014	16,000
				Peanuts, Potatoes	0.44		0.0017	0.0002	0.0019	12,000
				Dry/Succul. Beans, Lettuce	0.48		0.0018	0.0002	0.0020	11,000
				Fruit. Vegs	0.55		0.0021	0.0002	0.0023	9,500
				Canola	0.26	1,200	0.0033	0.0003	0.0036	6,100
Flagging for Aerial Application (7)	Baseline	0.011	0.35	Carrots	0.20	350	0.0017	0.0004	0.0021	10,000
				Stone Fruits, Tree Nuts, Pistachio	0.23		0.0019	0.0004	0.0023	9,500
				Bulb Veg.	0.30		0.0025	0.0005	0.0030	7,300
				Sm. Berries, Grapes, Strawberries	0.35		0.0029	0.0006	0.0035	6,200
				Peanuts, Potatoes	0.44		0.0036	0.0008	0.0044	5,000
				Dry/Succul. Beans, Lettuce	0.48		0.0040	0.0008	0.0048	4,500
				Fruit. Vegs	0.55		0.0045	0.0010	0.0055	4,000

Exposure Scenario (Scenario #)	Mitigation Level[a]	Dermal Unit Exposure[b] (mg/lb ai)	Inhalation Unit Exposure[c] (ug/lb ai)	Crop	Application Rate (lb ai/A)	Amount Treated[d] (A/day)	Daily Dermal Dose[e] (mg/kg/day)	Daily Inhalation Dose[f] (mg/kg/day)	Combined Daily Dose[g] (mg/kg/day)	MOE[h]
				Canola	0.26	1,200	0.0074	0.0016	0.0090	2,400

a Baseline consists of long-sleeve shirt, long pants, shoes, and socks and no respirator. PPE consists of long-sleeve shirt, long pants, shoes, socks, chemical-resistant gloves, and no respirator.
b Baseline Dermal Unit Exposure represents long pants, long sleeved shirt, no gloves, open mixing/loading, and open cab tractors, as appropriate.
c Baseline Inhalation Exposure represents no respiratory protection, open mixing/loading, and open cab tractors, as appropriate.
d Daily acres treated values are from EPA estimates of acreage that could be treated or volume handled in a single day for each exposure scenario of concern, based on the application method and formulation/packaging type.
e Daily dermal dose (mg/kg/d) = [unit dermal exposure (mg/lb ai) * dermal absorption (0.15) * application rate (lb ai/acre) * daily acres treated / body weight (70 kg).
f Daily inhalation dose (mg/kg/d) = (unit exposure (µg/lb ai) * (1mg/1000 µg) conversion * appl. rate (lb ai/acre) * daily acres treated / body weight (70 kg).
g Combined daily dose = daily dermal dose + daily inhalation dose.
h MOE = NOAEL (21.8 mg/kg/d) / combined daily dose. UF = 100.

The handler exposure estimates in this assessment are based on a central tendency estimate of unit exposure and an upper-percentile assumption for the application rate, and are assumed to be representative of high-end exposures. The uncertainties associated with this assessment stem from the use of surrogate exposure data (e.g., differences in use scenario and data confidence), and assumptions regarding that amount of chemical handled. The estimated exposures are believed to be reasonable high-end estimates based on observations from field studies and professional judgement.

7.2 Postapplication Exposure and Risk Estimates

It has been determined that there is a potential for occupational exposure from entering areas previously treated with BAS 510F. Post-application exposure scenarios associated with BAS 510 F are detailed in Table 7 in Attachment 6. Standard transfer coefficients (Tcs) were used based on the EPA Science Advisory Council for Exposure guidance on agricultural transfer coefficients (Policy 3.1, 08/07/00), and additional recently reviewed ARTF studies. Post-application exposure is expected to be short- and intermediate- term in duration.

Four dislodgeable foliar residue (DFR) studies (e.g. strawberries, grapes, peaches and tomatoes) were submitted in support of this registration action. PMRA performed primary reviews on the studies and HED performed secondary reviews. HED concurred with the DFR study reviews done by PMRA. A summary of each study and the assumptions used to estimate post-application exposure for these crops are provided in Attachment 6.

The occupational dermal post-application exposure and risk were calculated by coupling crop specific DFR values or turf TTR values with activity specific transfer coefficient (Tc) values from the HED Science Advisory Council For Exposure Policy Number 3.1: Agricultural Transfer Coefficients, August 2000.

For each DFR/TTR study, the site with the highest residue was selected for use in the risk assessment. The DFR studies were used to assess both crop specific as well as chemical specific surrogate data for determining post-application exposure for various other crops (i.e. leafy and root vegetables, cole crops and cucurbits). Table 15 summarizes the post-application exposure estimates for all crops. Post-application exposure estimates except for one, grapes with girdling, were all greater than the target MOE of 100 and therefore did not exceed HED's level of concern. The MOE for grapes with girdling was 95 on the day of application. The MOE did not reach the target MOE of 100 till day 9.

strawberry, blueberry, caneberry, rasberry	0	1.731 *	0.012	0.045	1800	490	0-days

Low/medium field row crops (peas, beans, canola, mint, and peanuts)	0	0.925 *	0.0016	0.040	14000	550	6-8 days - succulent peas 7-days - succulent beans 14 days - peanuts, mint 21 days - dry beans & peas, and canola,
Tall row crop (sunflower seeds)	0	0.920	0.0016	0.016	14000	1400	20-21 days
Deciduous fruit trees (stone fruits)	0	1.3	0.0022	0.067	9800	330	0-days
tree nuts	0	1.3	0.011	0.056	2000	390	14-days
cucurbits	0	0.597 *	0.0051	0.026	4300	850	0-days
fruiting vegetables	0	1.06	0.0091	0.018	2400	1200	0-days
cole crops	0	0.809 *	0.028	0.069	790	310	0-days 14-days
leafy vegetables	0	0.925 *	0.0079	0.04	2700	550	14-days
root vegetables	0	0.848 *	0.0044	0.036	5000	600	0-days - carrots and immature plants
							7-days - onions, garlic, leeks 30-days - potatoes
grapes w/girdling	0	1.343 *	0.012	0.23	1900	95	14-days
	2	1.327 *	0.011			96	
	4	1.31 *		0.22		97	
	5	1.3 *			2000	98	
	7	1.286 *				99	
	9	1.27 *				100	
blueberry, caneberry, rasberry; grapes w/o girdling	0	1.343 *	0.012	0.12	1900	190	
golf course turf	0	0.188	0.0016	0.053	14,000	410	N/A

1. * The highest daily average Dislodgeable Foliar Residues were adjusted for differences in application rates between the DFR studies and the proposed label rates

2. Daily dermal dose, = $\frac{\text{DFR, } (\mu g/cm^2) \times 1E\text{-}3 \text{ mg}/\mu g \times Tc \ (cm^2/hr) \times DA \times ET \ (hrs)}{BW \ (kg)}$

3. MOE = $\frac{\text{NOAEL (21.8 mg/kg/day)}}{\text{Dermal Daily Dose (mg/kg/day)}}$

Re-Entry Interval (REI)

Due to the statistical uncertainty in estimating the MOE, 95 is considered equivalent to the target of 100 for risk assessment in this case. Therefore, the Restricted Entry Interval (REI) may be based on acute toxicity of the active ingredient.

A 4-hour REI is proposed on the BAS 510 02F label. In accordance with the Federal Register Notice: Worker Protection Standard (WPS), Reduced REIs for Certain Pesticides (May 3, 1995), 4-hour REI active ingredients cannot be dermal sensitizers. The submitted dermal sensitization study

on guinea pigs (MRID# 45404819) was considered unacceptable and therefore the determination as to whether BAS 510F is or is not a dermal sensitizer could not be made. In addition, the data demonstrate that residues are highly persistent, dissipate slowly, and, for grape girdling, result in a MOE close to the level of concern. The technical material has a Toxicity Category III or IV. Per the WPS, a 12-hr REI is required. Therefore, **HED recommends use of the WPS required 12 hour REI based on acute toxicity categories and does not concur with the proposed 4-hour REI.** Should an acceptable dermal sensitizer study be submitted in the future, HED will revisit the REI issue.

8.0 DATA NEEDS

8.1 Toxicology

None.

8.2 Residue Chemistry

- Submission of a suitably **revised Section B**

1. Directions for Use on *Brassica* vegetables (subgroups 5A and 5B), cucurbit vegetables, mint, edible peas (use is allowed on any legume vegetable, except soybean, cowpea, field pea, and lupin), certain root vegetables (subgroup 1B, excluding use on garden beet, radish, and turnip at the petitioner's request) and sunflowers need to be added to the Endura™ and/or Pristine™ Fungicide labels. The label use pattern for each of these crops should be the same as that used in the crop field trials study which supports the target crop tolerance for that crop. Additionally, the applicable label(s) need to include a statement that use is prohibited on soybean, cowpea, field pea, and lupin; sugar beets, garden beets, turnips, and radishes.

2. Recropping (Plantback) Restrictions: The Endura™ and Pristine™ Fungicide labels need to include a statement that: "Crops with registered uses may be replanted at any time. All other crops grown for food or feed may be replanted after 14 days."

3. Maximum Seasonal Use Rate: As a precautionary measure, the Endura™ and Pristine™ Fungicide labels should include a statement to the effect that, if ever both these formulated products should be applied interchangeably to the same crop (i.e., same plants) during the growing of that crop, the total BAS 510 F ai/A applied to that crop is not to exceed that allowed had only one of these formulated products been used (i.e., ca 0.9-1.8 lbs ai/A total per season, depending on the specific crop).

- Submission of a suitably **revised Section F**

There are also several **conditions of registration** associated with the granting of these tolerances:

- **Conditions of Registration**

1. Submission of a radiovalidation study to support the adequacy of the proposed tolerance enforcement method (DFG S19) for livestock matrices (MRID 45405103). These

radiovalidation data will also be used in support of the data collection method (471/0) for livestock matrices (MRID 45405106).

2. Submission of radiovalidation data demonstrating the efficiency of the microwave hydrolysis step in Method 476/0, which determines bound residues of BAS 510 F in milk and liver (MRID 45405105).

3. Submission of all the proposed data collection and tolerance methods, revised to state that solutions of analytical standards should not be stored longer than 2 months before replacement. The proposed enforcement methods should also be revised in accordance with any comments made by ACL/BEAD arising from the TMV trials.

4. Submission of the Final Report of the storage stability study in plant matrices (MRID 45405109). The report should include a description of the fortification solutions (solvent) used in the study and a full description of the analytical method (445/0).

5. Submission of data demonstrating the frozen storage stability of BAS 510 F residues in processed grape juice (2 months) and tomato paste (5 months).

6. Submission of the following additional field trials, conducted per their respective proposed use pattern:

   - 3 for mustard greens (one each from Regions 2, 3, and 10)
   - 2 for cucumber (one each from Regions 2 and 10)
   - 1 for sunflower seed (from Region 5)

7. Submission of a limited field accumulation study (two sites) which provides residue data on beet tops (sugar or garden) and turnip tops, from beets and turnips planted as rotational crops into treated soil 14 days following the last of 3 applications of BAS 510 F totaling ~1.8 lbs ai/A. Provided those data show the rotational crop tolerance of 1.0 ppm for the leaves of root and tuber vegetables (crop group 2) is not exceeded, further studies would not be required.

8. Submission of a limited field accumulation study (two sites) which provides residue data on spinach and celery, planted as rotational crops into treated soil 14 days following the last of 3 applications of BAS 510 F totaling ~1.8 lbs ai/A. Provided those data show the 1.0 ppm rotational tolerance on crop group 4 (except lettuce) is not exceeded, further studies would not be required. Alternatively, the petitioner may submit a full set of crop field trials data for spinach (6) and celery (6), via a use pattern similar/identical to that for lettuce, and request a direct use tolerance on all of crop group 4.

Attachments:
1. HED HIARC report of 03/07/03, TXR No. 0051613;
2. HED Residue Summary memo of 08/15/03, M. Nelson, D278385;
3. HED MARC decision memo of 01/09/03, M. Nelson, D286786;
4. HED DEEM memo of 05/29/03, M. Doherty, D289724;
5. EFED memo of 09/16/02, C. Sutton, D278418;
6. HED ORE memo of 06/23/03, S. C. Wang, D290072.

cc with Attachments: Y.W. Donovan.
cc without Attachments: Maxie Nelson, Shih-Chi Wang, Alan Levy, Cheryl Sutton, RAB2 reading file, PP#1F06313.